EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	599	(544/158).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2007/03/13 09:28
L2	214	(514/239.2).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2007/03/13 09:26
L3	3	(("4956388") or ("5023269")).PN.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2007/03/13 09:28

Connecting via Winsock to STN

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LOGINID:SSSPTA1600RXA

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 4	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 6	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 7	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 8	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 9	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 10	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS 11	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS 12	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 13	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 14	DEC 18	CA/CAplus patent kind codes updated
NEWS 15	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 16	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 17	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS 18	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 19	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 20	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 21	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 22	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 23	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 24	JAN 29	PHAR reloaded with new search and display fields
NEWS 25	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 26	FEB 13	CASREACT coverage to be extended
NEWS 27	Feb 15	PATDPASPC enhanced with Drug Approval numbers
NEWS 28	Feb 15	RUSSIAPAT enhanced with pre-1994 records
NEWS 29	Feb 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS 30	Feb 26	MEDLINE reloaded with enhancements
NEWS 31	Feb 26	EMBASE enhanced with Clinical Trial Number field
NEWS 32	Feb 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS 33	Feb 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 34	Feb 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items

```
 NEWS IPC8      For general information regarding STN implementation of IPC 8
 NEWS X25       X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that
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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 08:16:01 ON 13 MAR 2007

=> fil reg
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.42       0.42

FILE 'REGISTRY' ENTERED AT 08:17:03 ON 13 MAR 2007
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STRUCTURE FILE UPDATES:   11 MAR 2007  HIGHEST RN 926007-42-3
DICTIONARY FILE UPDATES:  11 MAR 2007  HIGHEST RN 926007-42-3

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\QUERIES\10524798.str
```
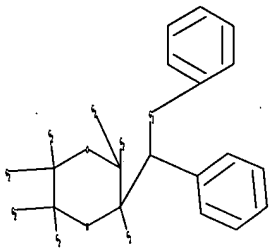
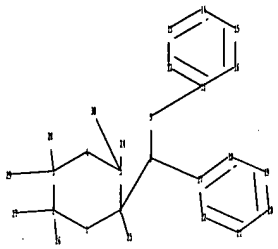





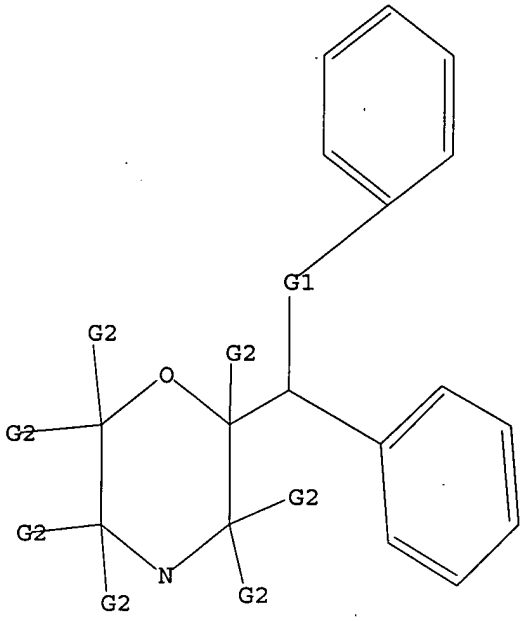
chain nodes :
8 9 24 25 26 27 28 29 30
ring nodes :
1 2 3 4 5 6 11 12 13 14 15 16 17 18 19 20 21 22
chain bonds :
2-26 2-27 3-28 3-29 5-24 5-30 6-25 6-8 8-17 8-9 9-11
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 11-12 11-16 12-13 13-14 14-15 15-16 17-18
17-22 18-19 19-20 20-21 21-22
exact/norm bonds :
1-2 1-6 2-3 2-26 2-27 3-4 3-28 3-29 4-5 5-6 5-24 5-30 6-25 8-9 9-11
exact bonds :
6-8 8-17
normalized bonds :
11-12 11-16 12-13 13-14 14-15 15-16 17-18 17-22 18-19 19-20 20-21 21-22
isolated ring systems :
containing 1 : 11 : 17 :

G1:O,S

G2:C,H

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 8:CLASS 9:CLASS 11:Atom 12:Atom
13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:Atom
22:Atom 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS

```
L1      STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1              STR
```



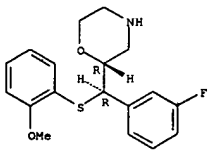

```
G1 O,S
G2 C,H

Structure attributes must be viewed using STN Express query preparation.


=> s l1
SAMPLE SEARCH INITIATED 08:17:20 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       75 TO ITERATE

100.0% PROCESSED       75 ITERATIONS                              38 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:           981 TO     2019
PROJECTED ANSWERS:              391 TO     1129

L2           38 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 08:17:35 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     1631 TO ITERATE

100.0% PROCESSED     1631 ITERATIONS                            851 ANSWERS
SEARCH TIME: 00.00.01

L3           851 SEA SSS FUL L1

=> s l3 and caplus/lc
      53707523 CAPLUS/LC
L4           738 L3 AND CAPLUS/LC

=> s l3 not l4
L5           113 L3 NOT L4
```

```
=> d l5 ed<2003
'ED<2003' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual
fields or predefined formats.  The predefined substance formats
are:  (RN = CAS Registry Number)

REG    - RN
SAM    - Index Name, MF, and structure - no RN
FIDE   - All substance data, except sequence data
IDE    - FIDE, but only 50 names
SQIDE  - IDE, plus sequence data
SQIDE3 - Same as SQIDE, but 3-letter amino acid codes are used
SQD    - Protein sequence data, includes RN
SQD3   - Same as SQD, but 3-letter amino acid codes are used
SQN    - Protein sequence name information, includes RN

CALC   - Table of calculated properties
EPROP  - Table of experimental properties
PROP   - EPROP and CALC

Any CA File format may be combined with any substance format to
obtain CA references citing the substance.  The substance formats
must be cited first.  The CA File predefined formats are:

ABS  -- Abstract
APPS -- Application and Priority Information
BIB  -- CA Accession Number, plus Bibliographic Data
CAN  -- CA Accession Number
CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
IND  -- Index Data
IPC  -- International Patent Classification
PATS -- PI, SO
STD  -- BIB, IPC, and NCL

IABS -- ABS, indented, with text labels
IBIB -- BIB, indented, with text labels
ISTD -- STD format, indented

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

The ALL format gives FIDE BIB ABS IND RE, plus sequence data when
it is available.
The MAX format is the same as ALL.
The IALL format is the same as ALL with BIB ABS and IND indented,
with text labels.

For additional information, please consult the following help
messages:

HELP DFIELDS -- To see a complete list of individual display fields.
HELP FORMATS -- To see detailed descriptions of the predefined formats.
ENTER DISPLAY FORMAT (IDE):end

=> s l5 ed<2003
MISSING OPERATOR

=> d his
```

```
     (FILE 'HOME' ENTERED AT 08:16:01 ON 13 MAR 2007)

     FILE 'REGISTRY' ENTERED AT 08:17:03 ON 13 MAR 2007
L1              STRUCTURE UPLOADED
L2           38 S L1
L3          851 S L1 FULL
L4          738 S L3 AND CAPLUS/LC
L5          113 S L3 NOT L4

=> s l5 and ed>2003
      29305412 ED>2003
                  (ED>20039999)
L6          112 L5 AND ED>2003

=> s l5 not l6
L7            1 L5 NOT L6

=> d l5 112-113
```

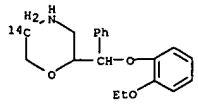
L5 ANSWER 112 OF 113 REGISTRY COPYRIGHT 2007 ACS on STN
RN 695815-31-7 REGISTRY
ED Entered STN: 18 Jun 2004
CN Morpholine, 2-[(R)-(3-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, (2R)-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C18 H20 F N O2 S
CI COM
SR CA

Absolute stereochemistry.

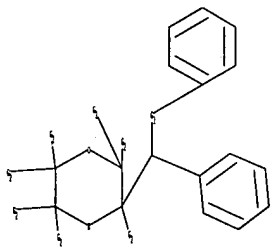


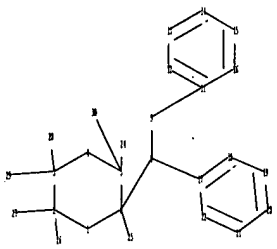
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L5 ANSWER 113 OF 113 REGISTRY COPYRIGHT 2007 ACS on STN
RN 135020-15-4 REGISTRY
ED Entered STN: 19 Jul 1991
CN Morpholine-3-14C, 6-[(2-ethoxyphenoxy)phenylmethyl]- (9CI) (CA INDEX NAME)
MF C19 H23 N O3
CI COM
SR CA



=>
Uploading C:\Program Files\Stnexp\Queries\QUERIES\10524798.str





chain nodes :
8 9 24 25 26 27 28 29 30
ring nodes :
1 2 3 4 5 6 11 12 13 14 15 16 17 18 19 20 21 22
chain bonds :
2-26 2-27 3-28 3-29 5-24 5-30 6-25 6-8 8-17 8-9 9-11
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 11-12 11-16 12-13 13-14 14-15 15-16 17-18
17-22 18-19 19-20 20-21 21-22
exact/norm bonds :
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exact bonds :
6-8 8-17
normalized bonds :
11-12 11-16 12-13 13-14 14-15 15-16 17-18 17-22 18-19 19-20 20-21 21-22
isolated ring systems :
containing 1 : 11 : 17 :

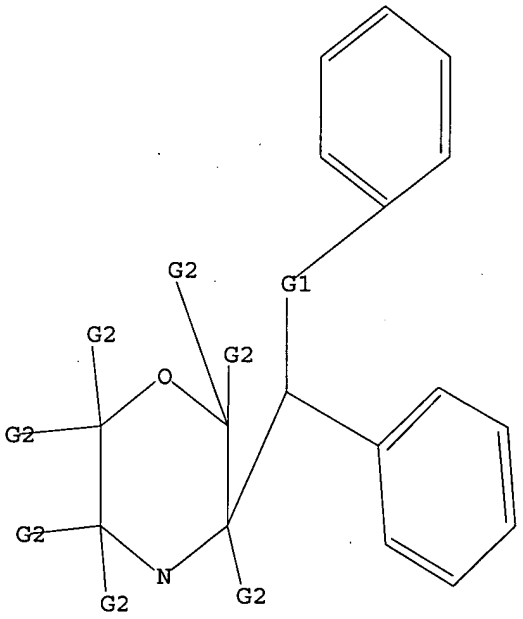
G1:O,S

G2:C,H

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 8:CLASS 9:CLASS 11:Atom 12:Atom
13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:Atom
22:Atom 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS

L8 STRUCTURE UPLOADED

=> d
L8 HAS NO ANSWERS
L8 STR



G1 O,S

G2 C,H

Structure attributes must be viewed using STN Express query preparation.

=> s l8
SAMPLE SEARCH INITIATED 08:20:19 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1 TO 80
PROJECTED ANSWERS: 0 TO 0

L9 0 SEA SSS SAM L8

=> s l8 full
FULL SEARCH INITIATED 08:20:22 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 30 TO ITERATE

100.0% PROCESSED 30 ITERATIONS 1 ANSWERS

```
SEARCH TIME: 00.00.01

L10             1 SEA SSS FUL L8

=> s l10 and caplus/lc
      53707523 CAPLUS/LC
L11           1 L10 AND CAPLUS/LC

=> fil caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                       364.75     365.17

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FILE COVERS 1907 - 13 Mar 2007  VOL 146 ISS 12
FILE LAST UPDATED: 11 Mar 2007  (20070311/ED)

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=> d his

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     FILE 'REGISTRY' ENTERED AT 08:17:03 ON 13 MAR 2007
L1                STRUCTURE UPLOADED
L2             38 S L1
L3            851 S L1 FULL
L4            738 S L3 AND CAPLUS/LC
L5            113 S L3 NOT L4
L6            112 S L5 AND ED>2003
L7              1 S L5 NOT L6
L8                STRUCTURE UPLOADED
L9              0 S L8
L10             1 S L8 FULL
L11             1 S L10 AND CAPLUS/LC

     FILE 'CAPLUS' ENTERED AT 08:20:32 ON 13 MAR 2007

=> s l11
L12           1 L11

=> d ibib abs hitstr
```

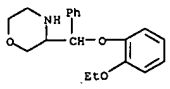
L12 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:238689 CAPLUS
DOCUMENT NUMBER: 142:291424
TITLE: Method for treatment of depression and anxiety disorders by combination therapy
INVENTOR(S): Arneric, Stephen P.; Clary, Cathryn M.; Feltner, Douglas; Harrison, Wilma M.; Kavoussi, Richard J.; Pande, Atul C.; Taylor, Charles Price
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 38 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005059654	A1	20050317	US 2004-935826	20040908
AU 2004271796	A1	20050324	AU 2004-271796	20040830
CA 2538412	A1	20050324	CA 2004-2538412	20040830
WO 2005025563	A1	20050324	WO 2004-IB2818	20040830
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1675582	A1	20060705	EP 2004-744329	20040830
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
BR 2004014347	A	20061107	BR 2004-14347	20040830
CN 1878546	A	20061213	CN 2004-80033396	20040830
JP 2007505095	T	20070308	JP 2006-525916	20040830
NO 2006001550	A	20060405	NO 2006-1550	20060405
PRIORITY APPLN. INFO.:			US 2003-502304P P	20030912
			WO 2004-IB2818 W	20040830

OTHER SOURCE(S): MARPAT 142:291424

AB A method is provided of treating depression in mammals, including a human, as well as depression and a concomitant disease, disorder or condition exemplified by, but not limited to, anxiety, sleep disorder and post-traumatic stress disorder. The method comprises administering to the mammal in effective amount a combination of active ingredients comprising (a) an alpha-2delta (A2D) ligand or a prodrug thereof, or a pharmaceutically acceptable salt of said A2D ligand or said prodrug and, active agents selected from; (b) a selective serotonin re-uptake inhibitor (SSRI) or a prodrug thereof or a pharmaceutically acceptable salt of said SSRI or said prodrug, (c) a selective noradrenaline re-uptake inhibitor (SNRI) or a prodrug thereof or a pharmaceutically acceptable salt of said SNRI or said prodrug and mixts. of (b) and (c). A pharmaceutical composition

L12 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
comprising a therapeutically effective amt. (a) an A2D ligand or a prodrug thereof, or a pharmaceutically acceptable salt of said A2D ligand or said prodrug and active agents selected from; (b) an SSRI or a prodrug thereof or a pharmaceutically acceptable salt of said SSRI or said prodrug, (c) an SNRI or a prodrug thereof or a pharmaceutically acceptable salt of said SNRI or said prodrug and mixts. of (b) and (c) is also provided. Preferred active ingredients for the treatment and the pharmaceutical compn. include pregabalin, gabapentin, sertraline and reboxetine.
IT 847832-28-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of depression and anxiety disorders by combination therapy)
RN 847832-28-4 CAPLUS
CN Morpholine, 3-[(2-ethoxyphenoxy)phenylmethyl]- (9CI) (CA INDEX NAME)



```
=> d his

     (FILE 'HOME' ENTERED AT 08:16:01 ON 13 MAR 2007)

     FILE 'REGISTRY' ENTERED AT 08:17:03 ON 13 MAR 2007
L1             STRUCTURE UPLOADED
L2          38 S L1
L3         851 S L1 FULL
L4         738 S L3 AND CAPLUS/LC
L5         113 S L3 NOT L4
L6         112 S L5 AND ED>2003
L7           1 S L5 NOT L6
L8             STRUCTURE UPLOADED
L9           0 S L8
L10          1 S L8 FULL
L11          1 S L10 AND CAPLUS/LC

     FILE 'CAPLUS' ENTERED AT 08:20:32 ON 13 MAR 2007
L12          1 S L11

=> s l4
L13        450 L4

=> fil reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       6.68     371.85

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                      -0.78      -0.78

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STRUCTURE FILE UPDATES:   11 MAR 2007  HIGHEST RN 926007-42-3
DICTIONARY FILE UPDATES:  11 MAR 2007  HIGHEST RN 926007-42-3

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> s l4 and 1/N
      5364956 1/N
L14        703 L4 AND 1/N
```
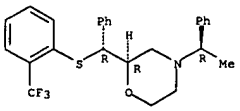

```
=> s l14 and 1-6/S
        8828697 1-6/S
L15          142 L14 AND 1-6/S

=> d scan
```

L15 142 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN Morpholine, 4-[(1R)-1-phenylethyl]-2-[(R)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2R)- (9CI)
MF C26 H26 F3 N O S

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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                                                          ENTRY    SESSION
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FILE LAST UPDATED: 11 Mar 2007  (20070311/ED)

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=> s l15
L16         42 L15

=> d ibib abs hitstr 1-42
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L16 ANSWER 1 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1144030 CAPLUS
DOCUMENT NUMBER: 145:495549
TITLE: Method and medicinal composition for curing neurasthenia and somatoform disorder
INVENTOR(S): Liu, Ping; Yu, Duo; Long, Haizhen; Li, Jintong; Li, Hua; Wang, Yu; Dai, Chengxiang; Chen, Guangliang; Xing, Houxun; Xu, Xiping
PATENT ASSIGNEE(S): Beijing Hafo Biomedical Research Center, Inc., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 21pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1850271	A	20061025	CN 2005-10064783	20050422
PRIORITY APPLN. INFO.:			CN 2005-10064783	20050422

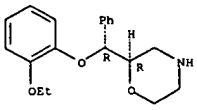
AB The medicinal composition for curing neurasthenia and somatoform disorder comprises medicinal dosage selective norepinephrine reuptake inhibitor (NARI) or its medicinal salts, and medicinal dosage selective serotonin (or 5-hydroxytryptamine) reuptake inhibitor (SSRI) or its medicinal acceptable salt composition The NARI comprises tomoxetine, reboxetine, bupropion, imipramine, desipramine, amitriptyline, nortriptyline, maprotiline and protriptyline, and reboxetine methane sulfonate. The SSRI comprises fluoxetine, sertraline, citalopram, paroxetine, fluvoxamine, sertraline hydrochloride, citalopram hydrobromide. The medicinal composition is prepared into oral preparation, i.v. injection or suppository. The somatoform disorder comprises somatoform disorder, hypochondria, somatoform autonomic dysfunction, persistent somatoform pain disorder.
IT 98769-84-7, Reboxetine mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method and medicinal composition for curing neurasthenia and somatoform disorder)
RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.

L16 ANSWER 1 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

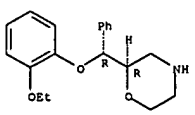
CRN 75-75-2
CMF C H4 O3 S

L16 ANSWER 2 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:804431 CAPLUS
DOCUMENT NUMBER: 145:195977
TITLE: A highly sensitive spectrofluorometric method for the determination of a new antidepressant drug, reboxetine, in tablets
AUTHOR(S): Onal, Armagan
CORPORATE SOURCE: Faculty of Pharmacy, Department of Analytical Chemistry, Istanbul University, Istanbul, 34116, Turk.
SOURCE: Journal of AOAC International (2006), 89(4), 972-975 CODEN: JAINEE; ISSN: 1060-3271
PUBLISHER: AOAC International
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A highly sensitive, selective, and rapid spectrofluorometric method was developed for the determination of reboxetine (REB) in tablets. The method is based on derivatization with 7-chloro-4-nitrobenzofurazan. The product showed an absorption maximum at 476 nm and a fluorescence emission peak at 533 nm in Et acetate. The optimum conditions of the reaction were investigated, and it was found that the reaction proceeded quant. at pH 8.5, 70°C in 5 min. The calibration graph is rectilinear over the range of 0.02-0.40 μg/mL. The relative standard deviation values for intraday and interday precision were 0.40-0.93 and 0.54-1.37%, resp. The proposed method was applied to the assay of REB in tablets. Mean recovery of REB from the tablets ranged between 99.91-100.20%. The results were compared statistically with those obtained by a method reported in the literature. The method is sensitive, simple, and selective, and can be used for routine quality control anal.
IT 98769-84-7, Edronax
RL: ANT (Analyte); RCT (Reactant); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(spectrofluorometric determination of reboxetine in tablets)
RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.



CM 2

CRN 75-75-2

L16 ANSWER 2 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CMF C H4 O3 S

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:739581 CAPLUS
DOCUMENT NUMBER: 146:197680
TITLE: Transfer of reboxetine into breastmilk, its plasma concentrations and lack of adverse effects in the breastfed infant
AUTHOR(S): Hackett, L. Peter; Ilett, Kenneth F.; Rampono, Jonathan; Kristensen, Judith H.; Kohan, Rolland
CORPORATE SOURCE: Clinical Pharmacology & Toxicology Laboratory, PathWest Laboratory Medicine, Nedlands, Australia
SOURCE: European Journal of Clinical Pharmacology (2006), 62(8), 633-638
CODEN: EJCPAS; ISSN: 0031-6970
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of this study was to investigate the transfer of reboxetine into milk, the absolute and relative infant doses via milk and to assess plasma concns. and adverse unwanted effects in the breastfed infant. Multiple samples of blood and milk were obtained over a dose interval at steady-state from four women who were taking reboxetine for postnatal depression. Drug concns. in plasma and milk were measured by high performance liquid chromatog. and milk/plasma ratio (M/P), absolute infant dose and relative infant dose were estimated by standard methods. Their four, breastfed, infants were also examined clin., and a blood sample was taken for drug anal. The median (range) dose taken by the women was 6 (4-10) mg/day. There was no significant difference in reboxetine concentration between paired fore-and hind-milk samples. The mean (95% CI) M/P was 0.06 (0.03, 0.09). Absolute infant dose was 1.7 (0.7, 2.4) μg/kg/day for reboxetine while the relative infant dose was 2.0% (1.3, 2.7%). Three of the infants met normal developmental milestones and no adverse effects were seen in any infant. The fourth infant had developmental problems that were not associated with the maternal reboxetine therapy. The concns. of reboxetine in plasma from the four infants were <4 μg/l, 2.6 μg/l, 2.3 μg/l and 5 μg/l, resp. The study suggests that reboxetine use by lactating women is safe for the breastfed infant. Nevertheless, our study had only four mother/baby pairs, and each decision to breastfeed should always be made on the basis of an individual risk/benefit anal.

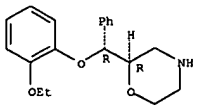
IT 98769-84-7, Edronax
RL: ADV (Adverse effect, including toxicity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reboxetine transfer into breastmilk, its plasma concns. and lack of adverse effects in breastfed infant)
RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.

L16 ANSWER 3 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:368900 CAPLUS
DOCUMENT NUMBER: 145:328137
TITLE: Efficacy and Tolerability of Reboxetine Compared with Citalopram: A Double-blind Study in Patients with Major Depressive Disorder
AUTHOR(S): Langworth, Sven; Bodlund, Owe; Aagren, Hans
CORPORATE SOURCE: Stockholm, Karolinska Institutet, and Pfizer Inc., Taeby, Swed.
SOURCE: Journal of Clinical Psychopharmacology (2006), 26(2), 121-127
CODEN: JCPYDR; ISSN: 0271-0749
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The objective of this study was to compare efficacy and tolerability of the selective noradrenalin reuptake inhibitor reboxetine with the selective serotonin reuptake inhibitor citalopram, in the treatment of major depressive disorder (MDD). In total, 357 outpatients with MDD were randomized to treatment with reboxetine 8-10 mg or citalopram 20-40 mg per day during 24 wk. Primary end-point was change from baseline in the Hamilton Depression Rating Scale (HAM-D, 21 items). Sexual function/dysfunction was measured by the Sexual Function scale (SF). Observed case anal. showed that both treatments yielded a gradual reduction of HAM-D scores: reboxetine with -21.4 and citalopram with -22.1 points (NS). LOCF anal. showed a greater reduction of the HAM-D scores with citalopram compared with reboxetine (-19.6 vs. -17.8; P = 0.034). The response rate was 90.3% for reboxetine and 92.7% for citalopram (NS). The most common side effect in the reboxetine group was dry mouth, and in the citalopram group sexual dysfunction. At week 24, anorgasmia was reported by 5.9% of the sexually active women in the reboxetine group vs 39% in the citalopram group. The dropout number was 91 in the reboxetine group, and 54 in the citalopram group. To summarize, both treatments gave a satisfactory antidepressant effect. The side effect profile differed between the groups, with a notably high prevalence of sexual dysfunctions in the citalopram group. The high number of dropouts in the reboxetine group, is considered as a result of the non-titration starting dose of 8 mg reboxetine per day, which gave a high incidence of early side-effects. Depressive disorders including major depression (MDD) is very common, with a lifetime prevalence of at least 15% in men and 25% in women. Depression can be treated effectively by a range of antidepressant agents. Recent reviews have suggested that the selective serotonin reuptake inhibitors (SSRIs) offer equal efficacy to the older antidepressant agents, such as tricyclic antidepressants, with the advantage of greater tolerability. Other reviewers have reported that non-SSRI antidepressants, such as clomipramine, have been found to be significantly more effective than fluoxetine for the treatment of patients with severe depression. Reboxetine (reboxetine mesylate, Edronax; Pfizer, New York) is a highly selective noradrenaline reuptake inhibitor, and the efficacy of reboxetine has been independently demonstrated in multiple randomized, double-blind, placebo-controlled studies. In addition to improvements in depressive symptoms, treatment-associated improvements in social behavior (measured using the Social Adaptation Self-evaluation Scale [SASS]), were noticed in one of these studies. In this study, reboxetine was statistically and clin. superior to both placebo and fluoxetine in improving social functioning. The primary objective of the current study was to assess efficacy and tolerability of reboxetine in comparison with those of citalopram (Cipramil; H. Lundbeck, Copenhagen, Denmark) in patients with MDD. Citalopram is a highly SSRI. The antidepressant mechanism is presumed to be a result of stimulation of serotonergic neurotransmission in the central nervous system as a consequence of higher serotonin levels resulting from inhibition of the serotonin transporter. The therapeutic efficacy of citalopram in patients with MDD has been investigated in several placebo-controlled studies and in long-term and extension studies. The underlying rationale for this comparison was to study 2 different drug profiles, 1 drug being pure 'adrenergic' and the other pure 'serotonergic'. A secondary objective was to analyze the correlation between the types of depression (ie, degree of melancholia and the efficacy of the 2 drugs).

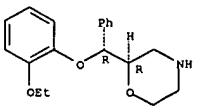
IT 98769-84-7, Edronax
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reboxetine and citalopram showed similar, clin. high satisfactory efficacy in response and remission rate in treatment of major depressive disorder patient)
RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.

L16 ANSWER 4 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 75-75-2
CMF C H4 O3 S

L16 ANSWER 4 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L16 ANSWER 5 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:301807 CAPLUS
DOCUMENT NUMBER: 144:343618
TITLE: Methods for regulating neurotransmitter systems by inducing counteradaptations
INVENTOR(S): Michalow, Alexander
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006034343	A2	20060330	WO 2005-US33826	20050923
WO 2006034343	A3	20061005		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 2006069086	A1	20060330	US 2005-234850	20050923
PRIORITY APPLN. INFO.:			US 2004-612155P	P 20040923

AB The present invention relates to methods for regulating neurotransmitter systems by inducing a counteradaptation response. According to one embodiment of the invention, a method for regulating a neurotransmitter includes the step of repeatedly administering a ligand for a receptor in the neurotransmitter system, with a ratio of administration half-life to period between administrations of no greater than 1/2. The methods of the present invention may be used to address a whole host of undesirable mental and neurol. conditions.

IT 98769-84-7, Edronax
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(regulating neurotransmitter systems by inducing counteradaptations by repeatedly administering neurotransmitter receptor ligands to treat mental and neurol. disorders and combination with other agents)

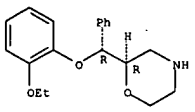
RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.

L16 ANSWER 5 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 75-75-2
CMF C H4 O3 S

L16 ANSWER 6 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1200904 CAPLUS
DOCUMENT NUMBER: 143:460166
TITLE: Preparation of morpholine derivatives for regulation of monoamine transporter function
INVENTOR(S): Fish, Paul Vincent; Mackenny, Malcolm Christian; Stobie, Alan; Wakenhut, Florian; Whitlock, Gavin Alistair
PATENT ASSIGNEE(S): UK
SOURCE: U.S. Pat. Appl. Publ., 88 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005250775	A1	20051110	US 2005-117896	20050428
PRIORITY APPLN. INFO.:			GB 2004-9744	A 20040430
			US 2004-576337P	P 20040602

OTHER SOURCE(S): MARPAT 143:460166
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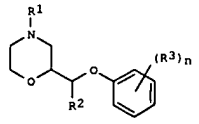

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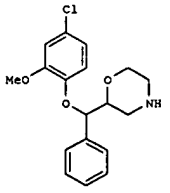


HCl

II

AB Title compds. I [R1 = H or alkyl; R2 = (un)substituted aryl, heterocycle, arylalkyl or R4; R3 each independently = alkyl, alkoxy, OH, halo, etc.; R4 = Ph group fused to a 5-6 membered carbocyclic group or heterocyclic group

L16 ANSWER 6 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
contg. at least one N, O or S atom;n = 0-4], and pharmaceutically acceptable salts thereof, are prepd. and disclosed as agents to regulate monoamine transporter function. Thus, e.g., II was prepd. by coupling of tert-Bu 2-[hydroxy(phenyl)methyl]morpholine-4-carboxylate (prepn. given) with 2-methoxy-4-chlorophenol followed by deprotection. In norepinephrine reuptake and serotonin reuptake inhibition assays, select I possessed Ki values less than 200 nM. I should prove useful as agents in the treatment of conditions including urinary disorders, pain, premature ejaculation, ADHD and fibromyalgia. Also provided are pharmaceutical compns. comprising one or more compds. of Formula I.

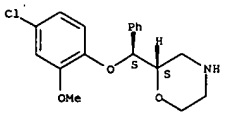
IT 869208-84-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of morpholine derivs. for regulation of monoamine transporter function)

RN 869208-84-4 CAPLUS
CN Morpholine, 2-[(S)-(4-chloro-2-methoxyphenoxy)phenylmethyl]-, (2S)-, sulfate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 869183-46-0
CMF C18 H20 Cl N O3

Absolute stereochemistry. Rotation (+).



CM 2

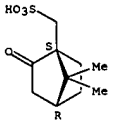
CRN 7664-93-9
CMF H2 O4 S

IT 869208-86-6P 869208-87-7P 869208-91-3P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(x-ray powder dif action anal.; preparation of morpholine derivs. for regulation of monoamine transporter function)

L16 ANSWER 6 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CRN 3144-16-9
CMF C10 H16 O4 S

Absolute stereochemistry. Rotation (+).

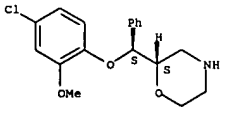


RN 869208-91-3 CAPLUS
CN 1,2-Ethanedisulfonic acid, compd. with (2S)-2-[(S)-(4-chloro-2-methoxyphenoxy)phenylmethyl]morpholine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 869183-46-0
CMF C18 H20 Cl N O3

Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-04-3
CMF C2 H6 O6 S2

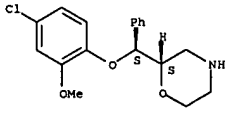
L16 ANSWER 6 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 869208-86-6 CAPLUS
CN Morpholine, 2-[(S)-(4-chloro-2-methoxyphenoxy)phenylmethyl]-, (2S)-, benzenesulfonate (9CI) (CA INDEX NAME)

CM 1

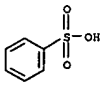
CRN 869183-46-0
CMF C18 H20 Cl N O3

Absolute stereochemistry. Rotation (+).



CM 2

CRN 98-11-3
CMF C6 H6 O3 S

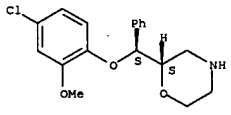


RN 869208-87-7 CAPLUS
CN Bicyclo[2.2.1]heptane-1-methanesulfonic acid, 7,7-dimethyl-2-oxo-, (1S,4R)-, compd. with (2S)-2-[(S)-(4-chloro-2-methoxyphenoxy)phenylmethyl]morpholine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 869183-46-0
CMF C18 H20 Cl N O3

Absolute stereochemistry. Rotation (+).



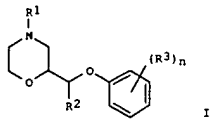
CM 2

L16 ANSWER 7 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

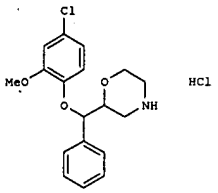
ACCESSION NUMBER:	2005:1200903 CAPLUS
DOCUMENT NUMBER:	143:460165
TITLE:	Preparation of morpholine derivatives for regulation of monoamine transporter function
INVENTOR(S):	Fish, Paul Vincent; Mackenny, Malcolm Christian; Stobie, Alan; Wakenhut, Florian; Whitlock, Gavin Alistair
PATENT ASSIGNEE(S):	Pfizer Limited, UK; Pfizer, Inc.
SOURCE:	PCT Int. Appl., 175 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005105100	A1	20051110	WO 2005-IB1154	20050420
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005237301	A1	20051110	AU 2005-237301	20050420
CA 2564990	A1	20051110	CA 2005-2564990	20050420
EP 1744754	A1	20070124	EP 2005-733458	20050420
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
NL 1028927	A1	20051103	NL 2005-1028927	20050429
NL 1028927	C2	20060427		
NO 2006004282	A	20061018	NO 2006-4282	20060921
PRIORITY APPLN. INFO.:			GB 2004-9744 A	20040430
			WO 2005-IB1154 W	20050420

OTHER SOURCE(S): MARPAT 143:460165
GI



I



II

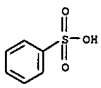
AB Title compds. I [R1 = H or alkyl; R2 = (un)substituted aryl, heterocycle, arylalkyl or R4; R3 each independently = alkyl, alkoxy, OH, halo, etc.; R4 = Ph group fused to a 5-6 membered carbocyclic group or heterocyclic group containing at least one N, O or S atom; n = 0-4], and pharmaceutically acceptable salts thereof, are prepared and disclosed as agents to regulate monoamine transporter function. Thus, e.g., II was prepared by coupling of tert-Bu 2-[hydroxy(phenyl)methyl]morpholine-4-carboxylate (preparation given) with 2-methoxy-4-chlorophenol followed by deprotection. In norepinephrine reuptake and serotonin reuptake inhibition assays, select I possessed Ki values less than 200 nM. I should prove useful as agents in the treatment of conditions including urinary disorders, pain, premature ejaculation, ADHD and fibromyalgia. Also provided are pharmaceutical compns. comprising one or more compds. of Formula I.

IT 869208-84-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of morpholine derivs. for regulation of monoamine transporter function)

RN 869208-84-4 CAPLUS
CN Morpholine, 2-[(S)-(4-chloro-2-methoxyphenoxy)phenylmethyl]-, (2S)-, sulfate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 98-11-3
CMF C6 H6 O3 S

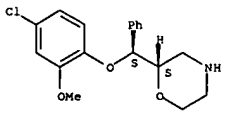


RN 869208-87-7 CAPLUS
CN Bicyclo[2.2.1]heptane-1-methanesulfonic acid, 7,7-dimethyl-2-oxo-, (1S,4R)-, compd. with (2S)-2-[(S)-(4-chloro-2-methoxyphenoxy)phenylmethyl]morpholine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 869183-46-0
CMF C18 H20 Cl N O3

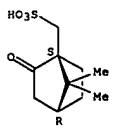
Absolute stereochemistry. Rotation (+).



CM 2

CRN 3144-16-9
CMF C10 H16 O4 S

Absolute stereochemistry. Rotation (+).



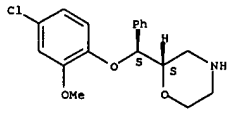
RN 869208-91-3 CAPLUS
CN 1,2-Ethanedisulfonic acid, compd. with (2S)-2-[(S)-(4-chloro-2-methoxyphenoxy)phenylmethyl]morpholine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 869183-46-0

CRN 869183-46-0
CMF C18 H20 Cl N O3

Absolute stereochemistry. Rotation (+).



CM 2

CRN 7664-93-9
CMF H2 O4 S

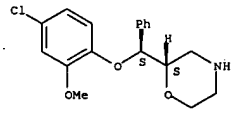
IT 869208-86-6P 869208-87-7P 869208-91-3P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(x-ray powder diffraction anal.; preparation of morpholine derivs. for regulation of monoamine transporter function)

RN 869208-86-6 CAPLUS
CN Morpholine, 2-[(S)-(4-chloro-2-methoxyphenoxy)phenylmethyl]-, (2S)-, benzenesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 869183-46-0
CMF C18 H20 Cl N O3

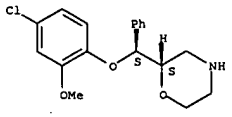
Absolute stereochemistry. Rotation (+).



CM 2

CMF C18 H20 Cl N O3

Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-04-3
CMF C2 H6 O6 S2

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 8 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1176480 CAPLUS
DOCUMENT NUMBER: 143:440426
TITLE: Substituted morpholine compounds for the treatment of central nervous system disorders, their preparation and pharmaceutical compositions
INVENTOR(S): Barta, Nancy S.; Glase, Shelly Ann; Gray, David L.; Reichard, Gregory A.; Simons, Lloyd J.; Xu, Weijan
PATENT ASSIGNEE(S): Warner-Lambert Company LLC, USA
SOURCE: U.S. Pat. Appl. Publ., 85 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005245519	A1	20051103	US 2005-119210	20050429
AU 2005238296	A1	20051110	AU 2005-238296	20050419
CA 2564994	A1	20051110	CA 2005-2564994	20050419
WO 2005105763	A1	20051110	WO 2005-IB1158	20050419
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1745029	A1	20070124	EP 2005-733459	20050419
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
NL 1028924	A1	20051101	NL 2005-1028924	20050429
NL 1028924	C2	20060427		
PRIORITY APPLN. INFO.:			US 2004-567244P P	20040430
			WO 2005-IB1158 W	20050419

OTHER SOURCE(S): MARPAT 143:440426
GI

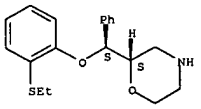
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to compds. of the formula I, which can be used in the treatment of central nervous system disorders. In compds. I, A is O or S; X is C1-10 alkyl, C2-8 alkenyl, aryl, heterocyclyl, C1-6 alkoxy, etc., with each group optionally substituted; and R1 - R5 are independently selected from H, OH, halo, C1-6 alkyl, aryl, C3-8 cycloalkyl, C2-6 alkenyl, C1-6 alkoxy, aryloxy, heterocyclyl, etc.; including pharmaceutically acceptable salts, enantiomers and diastereomers. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I and a pharmaceutically acceptable carrier, as well as to the use of the compns. in the treatment of central nervous system disorders. Ring opening of (R,R)-phenylglycidol with 1-naphthol followed by silylation of the primary alc., mesylation of the secondary alc., and desilylation gave mesylate II, which underwent ring closure to the epoxide, ring opening with ammonium hydroxide and amidation with chloroacetyl chloride, resulting in the formation of amide III. Compd. III was converted to the morpholine by intramol. cyclization and Red-Al redn. to give morpholine IV. Several compds., e.g., IV, express high inhibition of human norepinephrine transporter (hNET) and human serotonin transporter (hSERT).

IT 868685-38-5P 868686-05-9P 868686-06-0P
868687-84-7P 868687-85-8P 868687-91-6P,
2-[(2-Ethylsulfanylphenoxy)phenylmethyl]morpholine 868688-35-1P
868688-36-2P 868689-57-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of substituted morpholine compds. for treatment of CNS disorders)

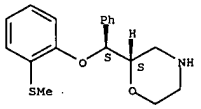
RN 868685-38-5 CAPLUS
CN Morpholine, 2-[(S)-[2-(ethylthio)phenoxy]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 868686-05-9 CAPLUS
CN Morpholine, 2-[(S)-[2-(methylthio)phenoxy]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

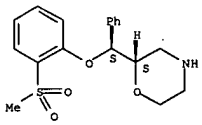
Absolute stereochemistry.



RN 868686-06-0 CAPLUS
CN Morpholine, 2-[(S)-[2-(methylsulfonyl)phenoxy]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

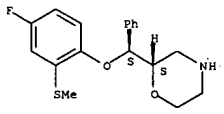
Absolute stereochemistry.

L16 ANSWER 8 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 868687-84-7 CAPLUS
CN Morpholine, 2-[(S)-[4-fluoro-2-(methylthio)phenoxy]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

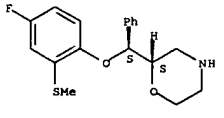


RN 868687-85-8 CAPLUS
CN Morpholine, 2-[(S)-[4-fluoro-2-(methylthio)phenoxy]phenylmethyl]-, (2S)-, (2E)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

CRN 868687-84-7
CMF C18 H20 F N O2 S

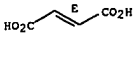
Absolute stereochemistry.



CM 2

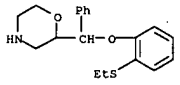
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

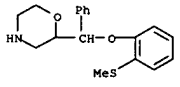


L16 ANSWER 8 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

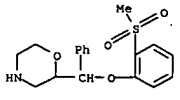
RN 868687-91-6 CAPLUS
CN Morpholine, 2-[[2-(ethylthio)phenoxy]phenylmethyl]- (9CI) (CA INDEX NAME)



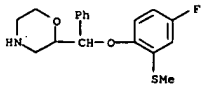
RN 868688-35-1 CAPLUS
CN Morpholine, 2-[[2-(methylthio)phenoxy]phenylmethyl]- (9CI) (CA INDEX NAME)



RN 868688-36-2 CAPLUS
CN Morpholine, 2-[[2-(methylsulfonyl)phenoxy]phenylmethyl]- (9CI) (CA INDEX NAME)



RN 868689-57-0 CAPLUS
CN Morpholine, 2-[[4-fluoro-2-(methylthio)phenoxy]phenylmethyl]- (9CI) (CA INDEX NAME)



L16 ANSWER 9 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1105437 CAPLUS
DOCUMENT NUMBER: 143:452076
TITLE: Equilibrium sampling through membrane based on a single hollow fibre for determination of drug-protein binding and free drug concentration in plasma
AUTHOR(S): Trtic-Petrovic, Tatjana; Liu, Jing-Fu; Joensson, Jan Aake
CORPORATE SOURCE: Vinca Institute of Nuclear Sciences, Laboratory of Physics, Belgrade, 11001,
SOURCE: Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2005), 826(1-2), 169-176
CODEN: JCBAAI; ISSN: 1570-0232
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The determination of drug-protein binding and free drug concentration in plasma applying the equilibrium sampling through membrane (ESTM) technique has been studied using supported liquid membrane extraction in a single hollow fiber without any membrane carrier. In the extraction setup, the donor phase (plasma or buffer) was placed in the vial, into which was immersed the hollow fiber with the acceptor phase situated in the lumen. This proposed technique was applied to study the drug-protein binding of five local anesthetics and two antidepressants as model substances, and the influence of the total drug concentration on the drug-protein binding was investigated. The brief theor. background for determination of the drug-protein binding under equilibrium conditions is described. The developed method shows a new, improved and simple procedure for determination of free drug concentration in plasma and extent of drug-protein binding.

IT 98769-84-7
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(equilibrium sampling through membrane based on a single hollow fiber for determination of drug-protein binding and free drug concentration in plasma)

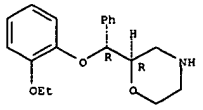
RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.

L16 ANSWER 9 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



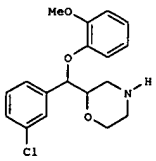
CM 2

CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 10 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:614812 CAPLUS
DOCUMENT NUMBER: 143:266876
TITLE: Enantioselective synthesis of (2R,3R)- and (2S,3S)-2-[(3-chlorophenyl)-(2-methoxyphenoxy)methyl]morpholine
AUTHOR(S): Harding, Wayne W.; Hodge, Matthis; Wang, Zhixia; Woolverton, William L.; Parrish, Damon; Deschamps, Jeffrey R.; Prisinzano, Thomas E.
CORPORATE SOURCE: College of Pharmacy, Division of Medicinal & Natural Products Chemistry, The University of Iowa, Iowa City, IA, 52242, USA
SOURCE: Tetrahedron: Asymmetry (2005), 16(13), 2249-2256
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:266876
GI



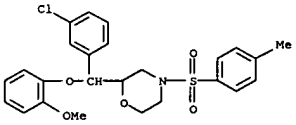
I

AB The enantioselective synthesis of the (R,R)- and (S,S)-enantiomers of I from com. available 3-chlorocinnamic acid is reported. The Sharpless asym. epoxidn. was used to establish the stereocenters in the synthesis of both enantiomers of I.

IT 863969-87-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of [chlorophenyl(methoxyphenoxy)methyl]arylsulfonylmorpholine and norepinephrine uptake inhibitory activity starting from chlorocinnamate using a multistep procedure)

RN 863969-87-3 CAPLUS
CN Morpholine, 2-[(3-chlorophenyl)(2-methoxyphenoxy)methyl]-4-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

L16 ANSWER 10 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



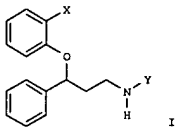
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 11 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:588645 CAPLUS
DOCUMENT NUMBER: 143:115550
TITLE: Preparation of heterocyclic compounds as selective norepinephrine reuptake inhibitors for treating hot flashes, impulse control disorders and personality change due to a general medical condition
INVENTOR(S): Allen, Albert John; Hemrick-Luecke, Susan; Sumner, Calvin Russell; Wallace, Owen Brendan
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 337 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005060949	A2	20050707	WO 2004-US38221	20041201
WO 2005060949	A3	20050909		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2548304	A1	20050707	CA 2004-2548304	20041201
EP 1729754	A2	20061213	EP 2004-811076	20041201
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 1889940	A	20070103	CN 2004-80036841	20041201
US 2007015786	A1	20070118	US 2006-581015	20060530
PRIORITY APPLN. INFO.:			US 2003-529428P	P 20031212
			WO 2004-US38221	W 20041201

OTHER SOURCE(S): MARPAT 143:115550
GI



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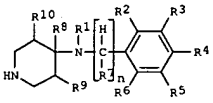


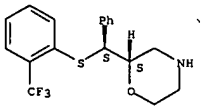
II

AB The invention relates to a method of preventing or treating hot flashes, vasomotor symptoms, impulse control disorders or personality change due to a general medical condition, comprising administering to a patient in need thereof a therapeutically effective amt. of a selective norepinephrine reuptake inhibitor selected from atomoxetine, reboxetine, I [X = alkylthio; Y = alkyl], II [n = 1-3; R1 = alkyl, alkenyl, cycloalkyl, etc.; R2-R4 = H, alkyl, alkoxy, etc.; R5-R6 = H, alkyl, alkoxy, halo; R7-R8 = H, alkyl; R9-R10 = H, halo, OH, CN, alkyl, alkoxy], etc. Over 200 title compds. such as I, II and other heterocyclic compds. disclosed, were prepd. E.g., a 2-step synthesis of N-(2-methylpropyl)-N-[(2-fluorophenyl)methyl]piperidin-4-amine fumarate, starting from tert-Bu 4-(2-methylpropylamino)piperidine-1-carboxylate and 2-fluorobenzaldehyde, was given. The preferred exemplified title compds. exhibit a Ki value less than 1 μM, more preferably less than 500 nM at the norepinephrine transporter as detd. using the scintillation proximity assay.

IT 668470-56-2P 668470-57-3P 668470-58-4P
668470-59-5P 668470-60-8P 668470-61-9P
668470-62-0P 668470-63-1P 668470-64-2P
668470-65-3P 668470-66-4P 668470-67-5P
668470-68-6P 668470-69-7P 668470-70-0P
668470-71-1P 668470-72-2P 668470-73-3P
668470-74-4P 668470-76-6P 668470-77-7P
668470-78-8P 668470-79-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic compds. as selective norepinephrine reuptake inhibitors for treating hot flashes, impulse control disorders and personality change due to general medical condition)

RN 668470-56-2 CAPLUS
CN Morpholine, 2-[(S)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)-(9CI) (CA INDEX NAME)

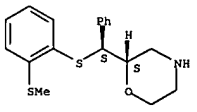
Absolute stereochemistry.



RN 668470-57-3 CAPLUS
CN Morpholine, 2-[(S)-[[2-(methylthio)phenyl]thio]phenylmethyl]-, (2S)-(9CI) (CA INDEX NAME)

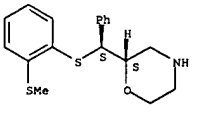
Absolute stereochemistry.

L16 ANSWER 11 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 668470-58-4 CAPLUS
CN Morpholine, 2-[(S)-[[2-(methylthio)phenyl]thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

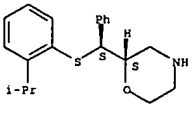
Absolute stereochemistry.



● HCl

RN 668470-59-5 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethyl)phenyl]thio]phenylmethyl]-, (2S)-(9CI) (CA INDEX NAME)

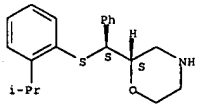
Absolute stereochemistry.



RN 668470-60-8 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethyl)phenyl]thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

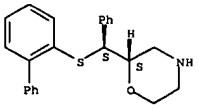
L16 ANSWER 11 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



● HCl

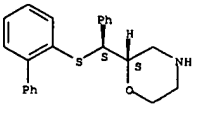
RN 668470-61-9 CAPLUS
CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-62-0 CAPLUS
CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

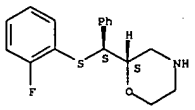
Absolute stereochemistry.



● HCl

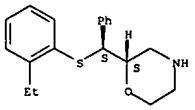
RN 668470-63-1 CAPLUS
CN Morpholine, 2-[(S)-[(2-fluorophenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



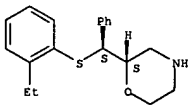
RN 668470-64-2 CAPLUS
CN Morpholine, 2-[(S)-[(2-ethylphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-65-3 CAPLUS
CN Morpholine, 2-[(S)-[(2-ethylphenyl)thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

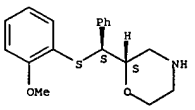
Absolute stereochemistry.

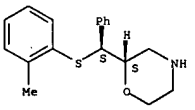


● HCl

RN 668470-66-4 CAPLUS
CN Morpholine, 2-[(S)-[(2-methoxyphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

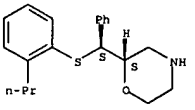
Absolute stereochemistry.





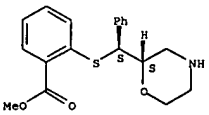
RN 668470-71-1 CAPLUS
CN Morpholine, 2-[(S)-phenyl[(2-propylphenyl)thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-72-2 CAPLUS
CN Benzoic acid, 2-[[(S)-(2S)-2-morpholinylphenylmethyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

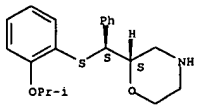


RN 668470-73-3 CAPLUS
CN Benzoic acid, 2-[[(S)-(2S)-2-morpholinylphenylmethyl]thio]-, methyl ester,
hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

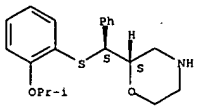
RN 668470-67-5 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-68-6 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

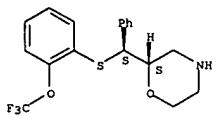
Absolute stereochemistry.



● HCl

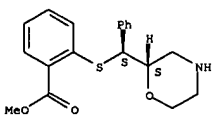
RN 668470-69-7 CAPLUS
CN Morpholine, 2-[(S)-phenyl[[2-(trifluoromethoxy)phenyl]thio]methyl]-, (2S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-70-0 CAPLUS
CN Morpholine, 2-[(S)-[(2-methylphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

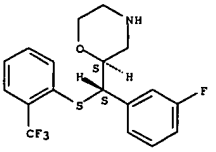
Absolute stereochemistry.



● HCl

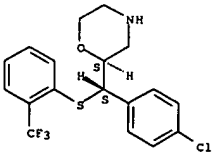
RN 668470-74-4 CAPLUS
CN Morpholine,
2-[(S)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



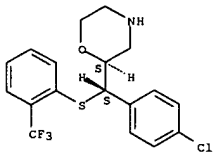
RN 668470-76-6 CAPLUS
CN Morpholine,
2-[(S)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-77-7 CAPLUS
CN Morpholine,
2-[(S)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

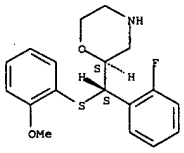
Absolute stereochemistry.



● HCl

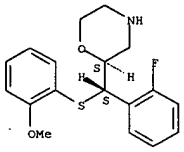
RN 668470-78-8 CAPLUS
CN Morpholine, 2-[(S)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-79-9 CAPLUS
CN Morpholine, 2-[(S)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

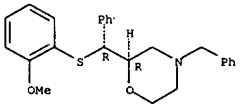


● HCl

IT 667876-61-1P 667876-73-5P 667876-84-8P

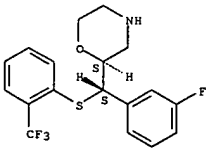
(2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 668470-75-5 CAPLUS
CN Morpholine,
2-[(S)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

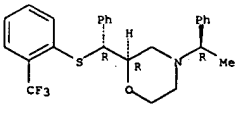
Absolute stereochemistry.



● HCl

RN 668470-88-0 CAPLUS
CN Morpholine, 4-[(1R)-1-phenylethyl]-2-[(R)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



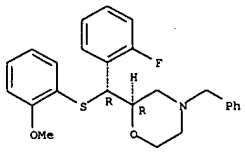
RN 668470-89-1 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(S)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

667876-86-0P 668470-75-5P 668470-88-0P
668470-89-1P 668470-90-4P 668470-91-5P
668470-92-6P 668470-95-9P 668470-97-1P
668471-00-9P 668471-02-1P 668471-04-3P
847687-22-3P 847687-24-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of heterocyclic compds. as selective norepinephrine reuptake inhibitors for treating hot flashes, impulse control disorders and personality change due to general medical condition)

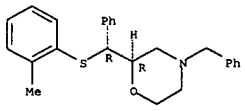
RN 667876-61-1 CAPLUS
CN Morpholine, 2-[(R)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



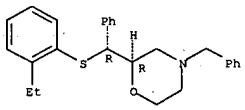
RN 667876-73-5 CAPLUS
CN Morpholine, 2-[(R)-[(2-methylphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 667876-84-8 CAPLUS
CN Morpholine, 2-[(R)-[(2-ethylphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 667876-86-0 CAPLUS
CN Morpholine,
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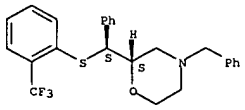
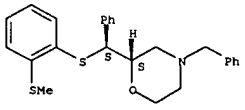


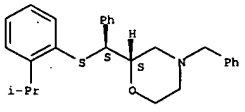
RN 668470-90-4 CAPLUS
CN Morpholine, 2-[(S)-[[2-(methylthio)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



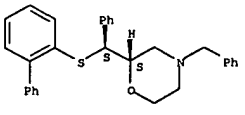
RN 668470-91-5 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethyl)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



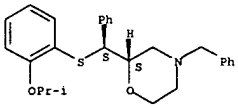
RN 668470-92-6 CAPLUS
CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



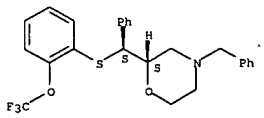
RN 668470-95-9 CAPLUS
CN Morpholine, 2-[(R)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



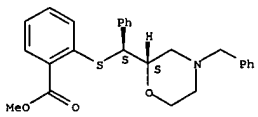
RN 668470-97-1 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(R)-phenyl[[2-(trifluoromethoxy)phenyl]thio]methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



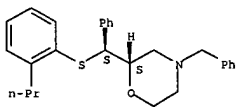
RN 668471-00-9 CAPLUS
CN Benzoic acid, 2-[[(R)-phenyl[(2R)-4-(phenylmethyl)-2-morpholinyl]methyl]thio]-, methyl ester, rel- (9CI) (CA INDEX NAME)

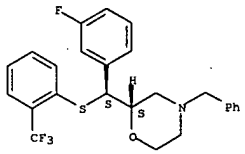
Relative stereochemistry.



RN 668471-02-1 CAPLUS
CN Morpholine, 2-[(R)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

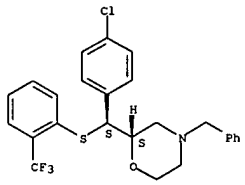
Relative stereochemistry.





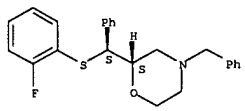
RN 668471-04-3 CAPLUS
CN Morpholine, 2-[(R)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 847687-22-3 CAPLUS
CN Morpholine, 2-[(R)-[(2-fluorophenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 847687-24-5 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(R)-phenyl[(2-propylphenyl)thio]methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

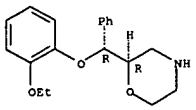
ACCESSION NUMBER: 2005:531541 CAPLUS
DOCUMENT NUMBER: 143:90865
TITLE: Chronic reboxetine desensitizes terminal but not somatodendritic α2-adrenoceptors controlling noradrenaline release in the rat dorsal hippocampus
AUTHOR(S): Parini, Stefania; Renoldi, Giuliano; Battaglia, Angelo; Invernizzi, Roberto W.
CORPORATE SOURCE: Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy
SOURCE: Neuropsychopharmacology (2005), 30(6), 1048-1055
CODEN: NEROEW; ISSN: 0893-133X
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The slow onset of antidepressant drugs' effects is thought to reflect the time required for the development of adaptive changes such as desensitization of presynaptic autoreceptors controlling the release of neurotransmitters. Using in vivo microdialysis in conscious rats, we studied the effect of a continuous infusion of the selective noradrenaline (NA) reuptake inhibitor reboxetine on extracellular concns. of NA. Doses of 10 mg/kg/day reboxetine through s.c. osmotic pumps for 2 days increased extracellular NA by 272% in the dorsal hippocampus (DH) of rats. NA rose significantly more in rats given reboxetine for 7 (469%) and 14 (437%) days. I.p. injection of 30 μg/kg clonidine, an α2-adrenoceptor agonist, reduced the release of NA to 49% of basal levels in rats given vehicle or reboxetine for 2 days, but this effect was markedly less in rats given reboxetine for 7 and 14 days. Likewise, the effect of intrahippocampal infusion of clonidine (0.05 and 0.2 μM) on extracellular NA was significantly attenuated in rats given reboxetine for 7 and 14 days, whereas the injection of 0.6 nmol clonidine into the locus coeruleus caused similar redns. of extracellular NA in the DH and prefrontal cortex (PFC) of rats infused with vehicle (DH -64%; PFC -42%) and reboxetine (DH -45%; PFC -28%) for 14 days. The results indicate that chronic treatment markedly enhances the effect of reboxetine on extracellular NA in the DH and suggest that this effect may be due to the desensitization of hippocampal α2-adrenoceptors.
IT 98769-84-7, Reboxetine mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chronic reboxetine methanesulfonate desensitizes terminal but not somatodendritic α2-adrenoceptor enhancing extracellular noradrenaline release in rat dorsal hippocampus)
RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.

L16 ANSWER 12 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L16 ANSWER 13 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

L16 ANSWER 13 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:529091 CAPLUS
DOCUMENT NUMBER: 143:393190
TITLE: Determination of Residual Organic Solvents in Reboxetine Mesylate by Capillary GC
AUTHOR(S): Lu, Dan
CORPORATE SOURCE: Shanghai Institute for Drug Control, Shanghai, 200233, Peop. Rep. China
SOURCE: Zhongguo Yiyao Gongye Zazhi (2004), 35(8), 492-493
CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER: Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB A simple capillary GC method for the determination of residual organic solvents, ethanol, dichloromethane, t-butanol, iso-Pr ether, Et acetate, 1,4-dioxane, pyridine and toluene, in reboxetine mesylate was established.
A DB-624 capillary column was used with procedural column temperature control.
The calibration curves were linear (r>0.99). The average recoveries were 86.6%-106.6%. The detection limites were 0.092-1.6 μg/mL.

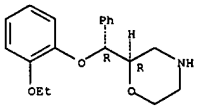
IT 98769-84-7, Reboxetine Mesylate
RL: AMX (Analytical matrix); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(determination of residual organic solvents in reboxetine mesylate by capillary GC)

RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

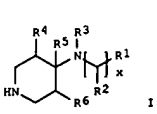
L16 ANSWER 14 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:523264 CAPLUS
DOCUMENT NUMBER: 143:59831
TITLE: A preparation of aminopiperidine derivatives, useful for the treatment of cognitive failure
INVENTOR(S): Hatfield, Alan Kramer; Bymaster, Franklin Porter; McKinzie, David Lee; Tucker, Tina Marie; Keaffaber, Kirk Matthew; Sumner, Calvin Russell; Trzepacz, Paula Terese; Allen, Albert John; Kelsey, Douglas Kenneth; Michelson, David; Gehlert, Donald Richard; Yang, Charles Renkin
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 300 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005053663	A2	20050616	WO 2004-US37195	20041124
WO 2005053663	A3	20050811		

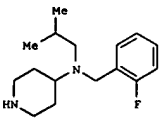
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-524450P P 20031124
US 2003-524781P P 20031125

OTHER SOURCE(S): MARPAT 143:59831
GI



I



II

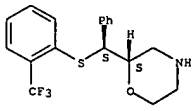
AB The invention relates to a preparation of aminopiperidine derivs. of formula I
[wherein: x is 1-3; R1 is (un)substituted phenyl; R2 and R5 are independently H or alkyl; R3 is (cyclo)alkyl, alkenyl, or cycloalkylalkyl,
etc.; R4 is H, halogen, or OH, etc.; R6 is H, halogen, CN, or alkyl,

L16 ANSWER 14 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
etc.], useful for the treatment of cognitive failure. Selective norepinephrine reuptake inhibitors were used to treat cognitive failure. For instance, fumarate salt of aminopiperidine deriv. II was prepd. via imination of 2-fluorobenzaldehyde by tert-Bu 4-[(2-methylpropyl)amino]piperidine-1-carboxylate, redn. of the obtained imine, and subsequent fumaric acid salt formation. The preferred invention compds. exhibit Ki values less than 500 nM at the norepinephrine transporter.

IT 668470-56-2P 668470-57-3P 668470-58-4P
668470-59-5P 668470-60-8P 668470-61-9P
668470-62-0P 668470-63-1P 668470-64-2P
668470-65-3P 668470-66-4P 668470-67-5P
668470-68-6P 668470-69-7P 668470-70-0P
668470-71-1P 668470-72-2P 668470-73-3P
668470-74-4P 668470-75-5P 668470-76-6P
668470-77-7P 668470-78-8P 668470-79-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminopiperidine derivs. useful for the treatment of cognitive failure)

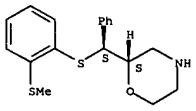
RN 668470-56-2 CAPLUS
CN Morpholine, 2-[(S)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



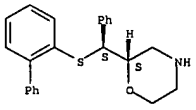
RN 668470-57-3 CAPLUS
CN Morpholine, 2-[(S)-[[2-(methylthio)phenyl]thio]phenylmethyl]-, (2S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



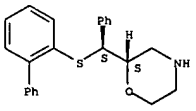
RN 668470-58-4 CAPLUS
CN Morpholine, 2-[(S)-[[2-(methylthio)phenyl]thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-62-0 CAPLUS
CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

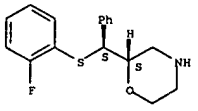
Absolute stereochemistry.



● HCl

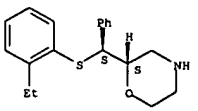
RN 668470-63-1 CAPLUS
CN Morpholine, 2-[(S)-[(2-fluorophenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

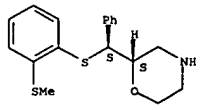
Absolute stereochemistry.



RN 668470-64-2 CAPLUS
CN Morpholine, 2-[(S)-[(2-ethylphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

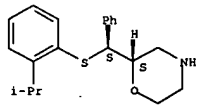




● HCl

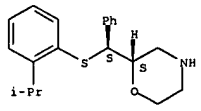
RN 668470-59-5 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethyl)phenyl]thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-60-8 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethyl)phenyl]thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



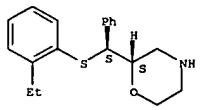
● HCl

RN 668470-61-9 CAPLUS
CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 668470-65-3 CAPLUS
CN Morpholine, 2-[(S)-[(2-ethylphenyl)thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

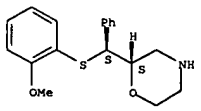
Absolute stereochemistry.



● HCl

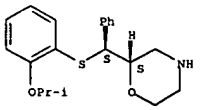
RN 668470-66-4 CAPLUS
CN Morpholine, 2-[(S)-[(2-methoxyphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



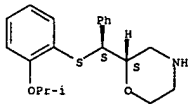
RN 668470-67-5 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-68-6 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

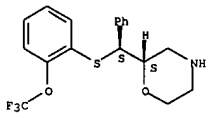
Absolute stereochemistry.



● HCl

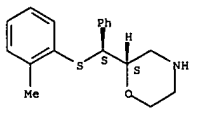
RN 668470-69-7 CAPLUS
CN Morpholine, 2-[(S)-phenyl[[2-(trifluoromethoxy)phenyl]thio]methyl]-, (2S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



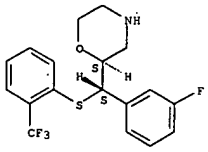
RN 668470-70-0 CAPLUS
CN Morpholine, 2-[(S)-[(2-methylphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



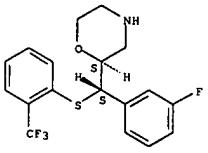
RN 668470-71-1 CAPLUS
CN Morpholine, 2-[(S)-phenyl[(2-propylphenyl)thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-75-5 CAPLUS
CN Morpholine,
2-[(S)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl
]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

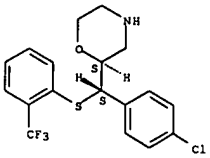
Absolute stereochemistry.



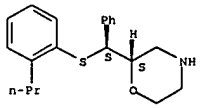
● HCl

RN 668470-76-6 CAPLUS
CN Morpholine,
2-[(S)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl
]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

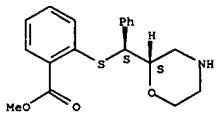


RN 668470-77-7 CAPLUS
CN Morpholine,
2-[(S)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl



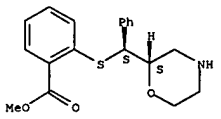
RN 668470-72-2 CAPLUS
CN Benzoic acid, 2-[[(S)-(2S)-2-morpholinylphenylmethyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-73-3 CAPLUS
CN Benzoic acid, 2-[[(S)-(2S)-2-morpholinylphenylmethyl]thio]-, methyl ester,
hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



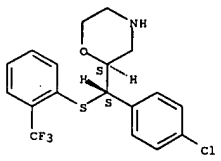
● HCl

RN 668470-74-4 CAPLUS
CN Morpholine,
2-[(S)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl
]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

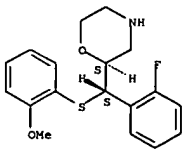
Absolute stereochemistry.



● HCl

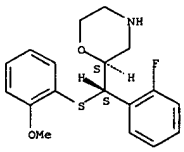
RN 668470-78-8 CAPLUS
CN Morpholine, 2-[(S)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, (2S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-79-9 CAPLUS
CN Morpholine, 2-[(S)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-,
hydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

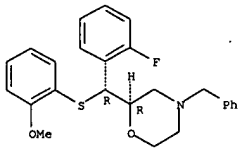


● HCl

IT 667876-61-1P 667876-73-5P 667876-84-8P
667876-86-0P 668470-88-0P 668470-89-1P
668470-90-4P 668470-91-5P 668470-92-6P
668470-95-9P 668470-97-1P 668471-00-9P
668471-02-1P 668471-04-3P 847687-22-3P
847687-24-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminopiperidine derivs. useful for the treatment of cognitive failure)

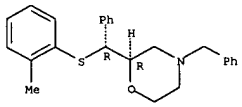
RN 667876-61-1 CAPLUS
CN Morpholine, 2-[(R)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



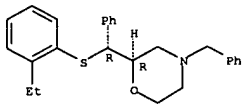
RN 667876-73-5 CAPLUS
CN Morpholine, 2-[(R)-[(2-methylphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



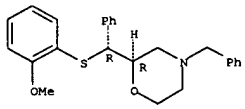
RN 667876-84-8 CAPLUS
CN Morpholine, 2-[(R)-[(2-ethylphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



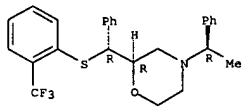
RN 667876-86-0 CAPLUS
CN Morpholine, 2-[(R)-[(2-methoxyphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



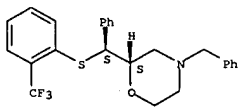
RN 668470-88-0 CAPLUS
CN Morpholine, 4-[(1R)-1-phenylethyl]-2-[(R)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



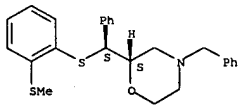
RN 668470-89-1 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(S)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



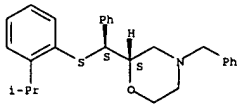
RN 668470-90-4 CAPLUS
CN Morpholine, 2-[(S)-[[2-(methylthio)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



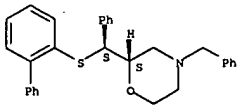
RN 668470-91-5 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethyl)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



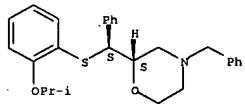
RN 668470-92-6 CAPLUS
CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



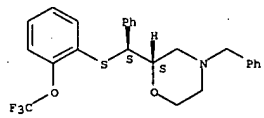
RN 668470-95-9 CAPLUS
CN Morpholine, 2-[(R)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



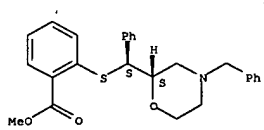
RN 668470-97-1 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(R)-phenyl[[2-(trifluoromethoxy)phenyl]thio]methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



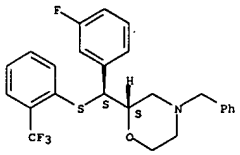
RN 668471-00-9 CAPLUS
CN Benzoic acid, 2-[[(R)-phenyl[(2R)-4-(phenylmethyl)-2-morpholinyl]methyl]thio]-, methyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



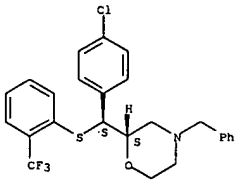
RN 668471-02-1 CAPLUS
CN Morpholine, 2-[(R)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



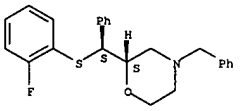
RN 668471-04-3 CAPLUS
CN Morpholine, 2-[(R)-(4-chlorophenyl)[(2-(trifluoromethyl)phenyl]thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



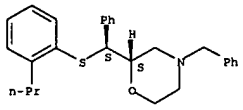
RN 847687-22-3 CAPLUS
CN Morpholine, 2-[(R)-[(2-fluorophenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 847687-24-5 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(R)-phenyl[(2-propylphenyl)thio]methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



ACCESSION NUMBER: 2005:216719 CAPLUS
DOCUMENT NUMBER: 142:291416
TITLE: Treatment of stuttering and other communication disorders with norepinephrine reuptake inhibitors
INVENTOR(S): Kelsey, Douglas Kenneth
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 299 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005021095	A2	20050310	WO 2004-US25591	20040825
WO 2005021095	A3	20050609		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2532349	A1	20050310	CA 2004-2532349	20040825
EP 1660185	A2	20060531	EP 2004-780429	20040825
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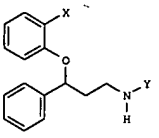
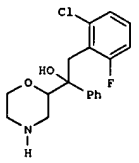
US 2007032554	A1	20070208	US 2006-568269	20060214
PRIORITY APPLN. INFO.:			US 2003-498018P P	20030827
			WO 2004-US25591 W	20040825

OTHER SOURCE(S): MARPAT 142:291416
GI



I



II

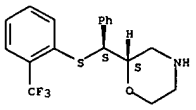
AB Provided are methods and medicaments for treating stuttering or another communication disorder, comprising administering to a patient in need of such treatment an effective amount of a selective norepinephrine reuptake inhibitor. The invention discloses the use of atomoxetine, racemic reboxetine, (S,S)-reboxetine, and compds. of formula I [wherein X = alkylthio and Y = alkyl; as described in U.S. patent Number 5,281,624], as well as their pharmaceutically acceptable salts, as the norepinephrine reuptake inhibitors described for treatment purposes. The invention further discloses the preparation of addnl. heterocyclic derivs. (as well as their pharmaceutically acceptable salts) that possess ability to serve as norepinephrine reuptake inhibitors. For instance, morpholine derivative II•HCl was prepared via alkylation of (4-benzyl-morpholin-2-yl)(phenyl)methanone with 2-chloro-6-fluorobenzylmagnesium chloride and subsequent N-debenzylation. The preferred invention compds. exhibited Ki values of less than 500 nM at the norepinephrine transporter (scintillation proximity assay).

IT 668470-56-2P 668470-57-3P 668470-58-4P
668470-59-5P 668470-60-8P 668470-61-9P
668470-62-0P 668470-63-1P 668470-64-2P
668470-65-3P 668470-66-4P 668470-67-5P
668470-68-6P 668470-69-7P 668470-70-0P
668470-71-1P 668470-72-2P 668470-73-3P
668470-74-4P 668470-75-5P 668470-76-6P
668470-77-7P 668470-78-8P 668470-79-9P
847687-23-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic compds. useful as norepinephrine reuptake inhibitors)

RN 668470-56-2 CAPLUS

CN Morpholine, 2-[(S)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)-(9CI) (CA INDEX NAME)

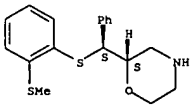
Absolute stereochemistry.



RN 668470-57-3 CAPLUS

CN Morpholine, 2-[(S)-[[2-(methylthio)phenyl]thio]phenylmethyl]-, (2S)-(9CI) (CA INDEX NAME)

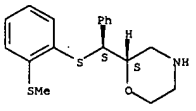
Absolute stereochemistry.



RN 668470-58-4 CAPLUS

CN Morpholine, 2-[(S)-[[2-(methylthio)phenyl]thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

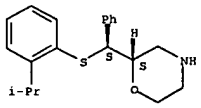


● HCl

RN 668470-59-5 CAPLUS

CN Morpholine, 2-[(S)-[[2-(1-methylethyl)phenyl]thio]phenylmethyl]-, (2S)-(9CI) (CA INDEX NAME)

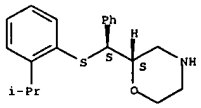
Absolute stereochemistry.



RN 668470-60-8 CAPLUS

CN Morpholine, 2-[(S)-[[2-(1-methylethyl)phenyl]thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

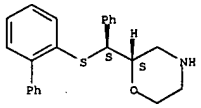


● HCl

RN 668470-61-9 CAPLUS

CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

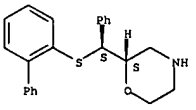
Absolute stereochemistry.



RN 668470-62-0 CAPLUS

CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

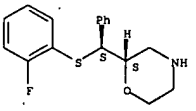


● HCl

RN 668470-63-1 CAPLUS

CN Morpholine, 2-[(S)-[(2-fluorophenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

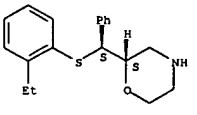
Absolute stereochemistry.



RN 668470-64-2 CAPLUS

CN Morpholine, 2-[(S)-[(2-ethylphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

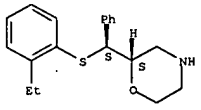
Absolute stereochemistry.



RN 668470-65-3 CAPLUS

CN Morpholine, 2-[(S)-[(2-ethylphenyl)thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

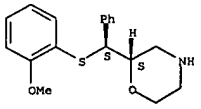


● HCl

RN 668470-66-4 CAPLUS

CN Morpholine, 2-[(S)-[(2-methoxyphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

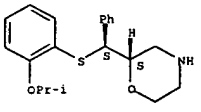
Absolute stereochemistry.



RN 668470-67-5 CAPLUS

CN Morpholine, 2-[(S)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-, (2S)-(9CI) (CA INDEX NAME)

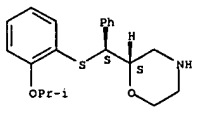
Absolute stereochemistry.



RN 668470-68-6 CAPLUS

CN Morpholine, 2-[(S)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

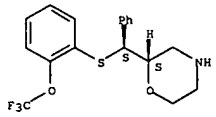
Absolute stereochemistry.



● HCl

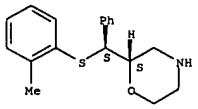
RN 668470-69-7 CAPLUS
CN Morpholine, 2-[(S)-phenyl[[2-(trifluoromethoxy)phenyl]thio]methyl]-, (2S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



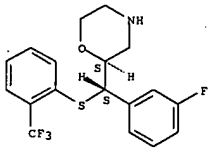
RN 668470-70-0 CAPLUS
CN Morpholine, 2-[(S)-[(2-methylphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



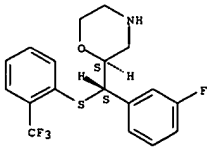
RN 668470-71-1 CAPLUS
CN Morpholine, 2-[(S)-phenyl[(2-propylphenyl)thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-75-5 CAPLUS
CN Morpholine,
2-[(S)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl
]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

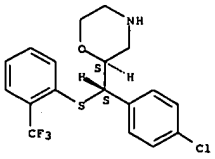
Absolute stereochemistry.



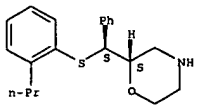
● HCl

RN 668470-76-6 CAPLUS
CN Morpholine,
2-[(S)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl
]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

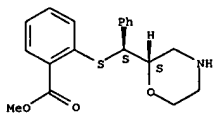


RN 668470-77-7 CAPLUS
CN Morpholine,
2-[(S)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl



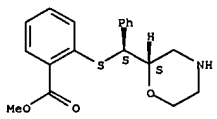
RN 668470-72-2 CAPLUS
CN Benzoic acid, 2-[[(S)-(2S)-2-morpholinylphenylmethyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-73-3 CAPLUS
CN Benzoic acid, 2-[[(S)-(2S)-2-morpholinylphenylmethyl]thio]-, methyl ester,
hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



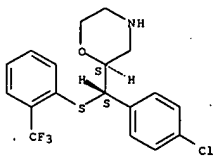
● HCl

RN 668470-74-4 CAPLUS
CN Morpholine,
2-[(S)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl
]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

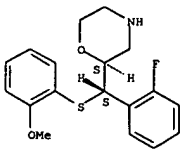
Absolute stereochemistry.



● HCl

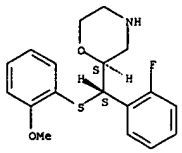
RN 668470-78-8 CAPLUS
CN Morpholine, 2-[(S)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, (2S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-79-9 CAPLUS
CN Morpholine, 2-[(S)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-,
hydrochloride, (2S)- (9CI) (CA INDEX NAME)

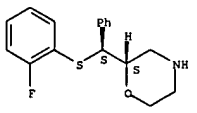
Absolute stereochemistry.



● HCl

RN 847687-23-4 CAPLUS
CN Morpholine, 2-[(S)-[(2-fluorophenyl)thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

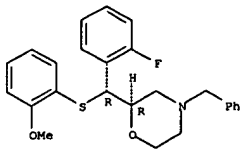
Absolute stereochemistry.



● HCl

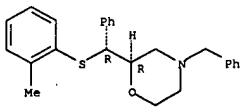
IT 667876-61-1P 667876-73-5P 667876-84-8P
667876-86-0P 668470-88-0P 668470-89-1P
668470-90-4P 668470-91-5P 668470-92-6P
668470-95-9P 668470-97-1P 668471-00-9P
668471-02-1P 668471-04-3P 847687-22-3P
847687-24-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclic compds. useful as norepinephrine reuptake inhibitors)
RN 667876-61-1 CAPLUS
CN Morpholine, 2-[(R)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



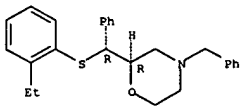
RN 667876-73-5 CAPLUS
CN Morpholine, 2-[(R)-[(2-methylphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



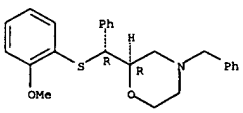
RN 667876-84-8 CAPLUS
CN Morpholine, 2-[(R)-[(2-ethylphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 667876-86-0 CAPLUS
CN Morpholine,
2-[(R)-[(2-methoxyphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

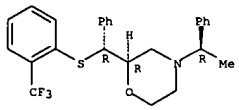
Relative stereochemistry.



RN 668470-88-0 CAPLUS

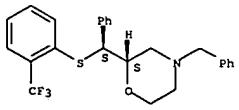
CN Morpholine, 4-[(1R)-1-phenylethyl]-2-[(R)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



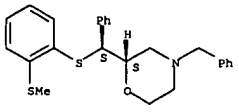
RN 668470-89-1 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(S)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



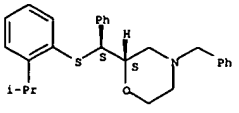
RN 668470-90-4 CAPLUS
CN Morpholine, 2-[(S)-[[2-(methylthio)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-91-5 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethyl)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

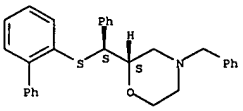
Absolute stereochemistry.



RN 668470-92-6 CAPLUS

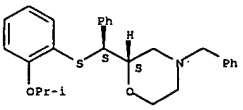
CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



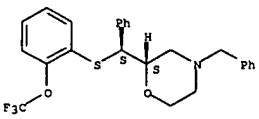
RN 668470-95-9 CAPLUS
CN Morpholine, 2-[(R)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



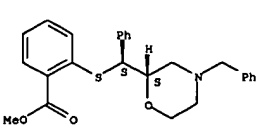
RN 668470-97-1 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(R)-phenyl[[2-(trifluoromethoxy)phenyl]thio]methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



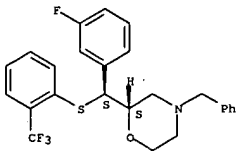
RN 668471-00-9 CAPLUS
CN Benzoic acid, 2-[[(R)-phenyl[(2R)-4-(phenylmethyl)-2-morpholinyl]methyl]thio]-, methyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



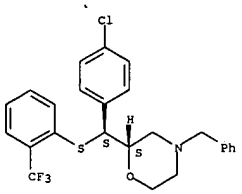
RN 668471-02-1 CAPLUS
CN Morpholine,
2-[(R)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl
]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



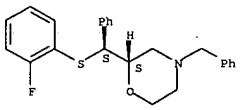
RN 668471-04-3 CAPLUS
CN Morpholine,
2-[(R)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl
]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 847687-22-3 CAPLUS
CN Morpholine, 2-[(R)-[(2-fluorophenyl)thio]phenylmethyl]-4-(phenylmethyl)-,
(2R)-rel- (9CI) (CA INDEX NAME)

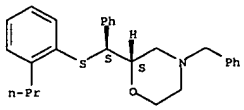
Relative stereochemistry.



RN 847687-24-5 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(R)-phenyl[(2-propylphenyl)thio]methyl]-,

(2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



ACCESSION NUMBER: 2005:216660 CAPLUS
DOCUMENT NUMBER: 142:291415
TITLE: Treatment of pervasive development disorders employing
norepinephrine reuptake inhibitors
INVENTOR(S): Allen, Albert John; Kelsey, Douglas Kenneth
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 300 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005020976	A2	20050310	WO 2004-US25593	20040825
WO 2005020976	A3	20050616		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2536161	A1	20050310	CA 2004-2536161	20040825
EP 1660065	A2	20060531	EP 2004-780431	20040825
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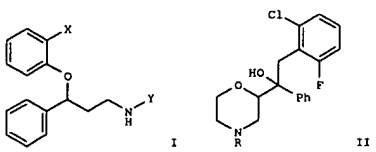
US 20062411 88	A1	20061026	US 2006-568466	20060214
PRIORITY APPLN. INFO.:			US 2003-498146P	P 20030827
			WO 2004-US25593	W 20040825

OTHER SOURCE(S): MARPAT 142:291415
GI



I II

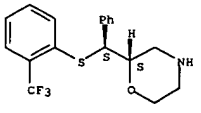
AB Provided are methods and medicaments for treating a pervasive development disorder, comprising administering to a patient in need of such treatment an effective amount of a selective norepinephrine reuptake inhibitor.
The

invention discloses the use of atomoxetine, racemic reboxetine, (S,S)-reboxetine, and compds. of formula I [wherein X = alkylthio and Y = alkyl; as described in U.S. patent No. 5,281,624], as well as their pharmaceutically acceptable salts, as the norepinephrine reuptake inhibitors described for treatment purposes. The invention further discloses the prepn. of addnl. heterocyclic derivs. (as well as their pharmaceutically acceptable salts) that possess ability to serve as norepinephrine reuptake inhibitors. For instance, morpholine deriv. II•HCl (R = H) was prepd. via alkylation of (4-benzyl-morpholin-2-yl)(phenyl)methanone by 2-chloro-6-fluorobenzylmagnesium chloride and subsequent N-debenzylation of the obtained alc. I (R = Bn). The preferred
invention compds. exhibited Ki values of less than 500 nM at the norepinephrine transporter (scintillation proximity assay).

IT 668470-56-2P 668470-57-3P 668470-58-4P
668470-59-5P 668470-60-8P 668470-61-9P
668470-62-0P 668470-63-1P 668470-64-2P
668470-65-3P 668470-66-4P 668470-67-5P
668470-68-6P 668470-69-7P 668470-70-0P
668470-71-1P 668470-72-2P 668470-73-3P
668470-74-4P 668470-75-5P 668470-76-6P
668470-77-7P 668470-78-8P 668470-79-9P
847687-23-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic compds. useful as norepinephrine reuptake inhibitors)

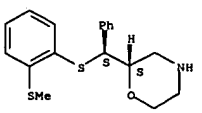
RN 668470-56-2 CAPLUS
CN Morpholine, 2-[(S)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-57-3 CAPLUS
CN Morpholine, 2-[(S)-[[2-(methylthio)phenyl]thio]phenylmethyl]-, (2S)-(9CI)
(CA INDEX NAME)

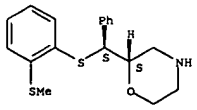
Absolute stereochemistry.



RN 668470-58-4 CAPLUS

L16 ANSWER 16 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Morpholine, 2-[(S)-[[2-(methylthio)phenyl]thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

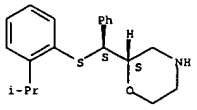
Absolute stereochemistry.



● HCl

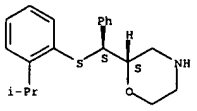
RN 668470-59-5 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethyl)phenyl]thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-60-8 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethyl)phenyl]thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



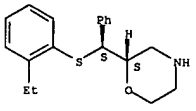
● HCl

RN 668470-61-9 CAPLUS
CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L16 ANSWER 16 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Morpholine, 2-[(S)-[(2-ethylphenyl)thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

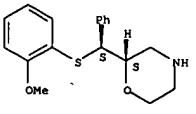
Absolute stereochemistry.



● HCl

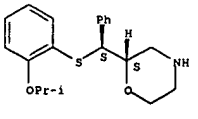
RN 668470-66-4 CAPLUS
CN Morpholine, 2-[(S)-[(2-methoxyphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



RN 668470-67-5 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

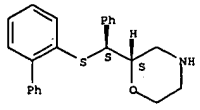
Absolute stereochemistry.



RN 668470-68-6 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

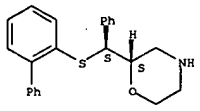
Absolute stereochemistry.

L16 ANSWER 16 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 668470-62-0 CAPLUS
CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

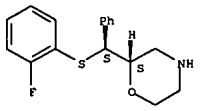
Absolute stereochemistry.



● HCl

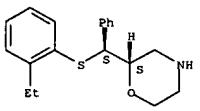
RN 668470-63-1 CAPLUS
CN Morpholine, 2-[(S)-[(2-fluorophenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



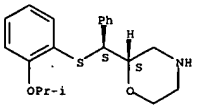
RN 668470-64-2 CAPLUS
CN Morpholine, 2-[(S)-[(2-ethylphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-65-3 CAPLUS

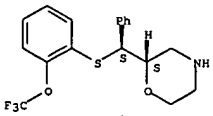
L16 ANSWER 16 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



● HCl

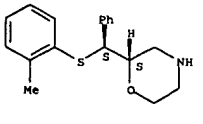
RN 668470-69-7 CAPLUS
CN Morpholine, 2-[(S)-phenyl[[2-(trifluoromethoxy)phenyl]thio]methyl]-, (2S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



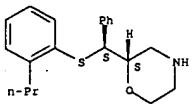
RN 668470-70-0 CAPLUS
CN Morpholine, 2-[(S)-[(2-methylphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



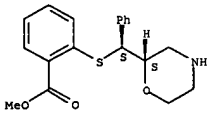
RN 668470-71-1 CAPLUS
CN Morpholine, 2-[(S)-phenyl[(2-propylphenyl)thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



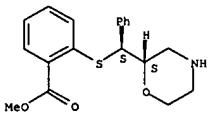
RN 668470-72-2 CAPLUS
CN Benzoic acid, 2-[[(S)-(2S)-2-morpholinylphenylmethyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-73-3 CAPLUS
CN Benzoic acid, 2-[[(S)-(2S)-2-morpholinylphenylmethyl]thio]-, methyl ester,
hydrochloride (9CI) (CA INDEX NAME)

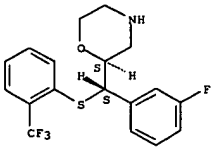
Absolute stereochemistry.



● HCl

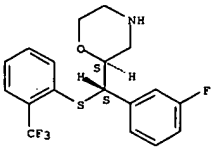
RN 668470-74-4 CAPLUS
CN Morpholine,
2-[(S)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-75-5 CAPLUS
CN Morpholine,
2-[(S)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

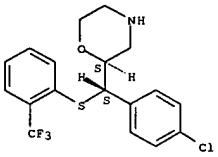
Absolute stereochemistry.



● HCl

RN 668470-76-6 CAPLUS
CN Morpholine,
2-[(S)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

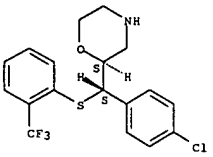
Absolute stereochemistry.



RN 668470-77-7 CAPLUS
CN Morpholine,
2-[(S)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl

]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

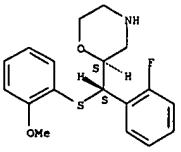
Absolute stereochemistry.



● HCl

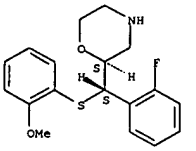
RN 668470-78-8 CAPLUS
CN Morpholine, 2-[(S)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-79-9 CAPLUS
CN Morpholine, 2-[(S)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

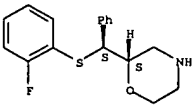
Absolute stereochemistry.



● HCl

RN 847687-23-4 CAPLUS
CN Morpholine, 2-[(S)-[(2-fluorophenyl)thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

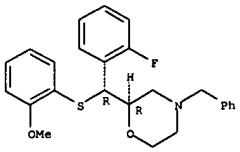


● HCl

IT 667876-61-1P 667876-73-5P 667876-84-8P
667876-86-0P 668470-88-0P 668470-89-1P
668470-90-4P 668470-91-5P 668470-92-6P
668470-95-9P 668470-97-1P 668471-00-9P
668471-02-1P 668471-04-3P 847687-22-3P
847687-24-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclic compds. useful as norepinephrine reuptake inhibitors)

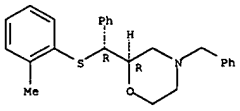
RN 667876-61-1 CAPLUS
CN Morpholine, 2-[(R)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



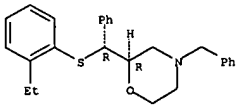
RN 667876-73-5 CAPLUS
CN Morpholine, 2-[(R)-[(2-methylphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



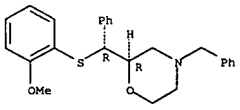
RN 667876-84-8 CAPLUS
CN Morpholine, 2-[(R)-[(2-ethylphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 667876-86-0 CAPLUS
CN Morpholine,
2-[(R)-[(2-methoxyphenyl)thio]phenylmethyl]-4-(phenylmethyl)-,.
(2R)-rel- (9CI) (CA INDEX NAME)

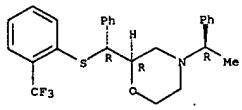
Relative stereochemistry.



RN 668470-88-0 CAPLUS

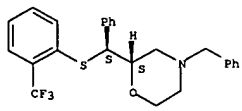
CN Morpholine, 4-[(1R)-1-phenylethyl]-2-[(R)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



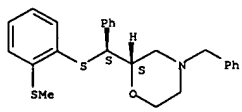
RN 668470-89-1 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(S)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



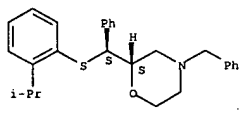
RN 668470-90-4 CAPLUS
CN Morpholine, 2-[(S)-[[2-(methylthio)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-91-5 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethyl)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

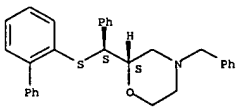
Absolute stereochemistry.



RN 668470-92-6 CAPLUS

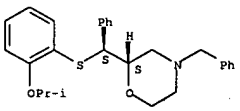
CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



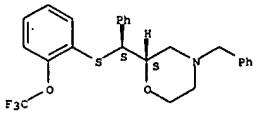
RN 668470-95-9 CAPLUS
CN Morpholine, 2-[(R)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



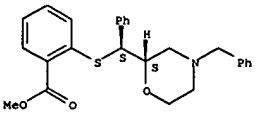
RN 668470-97-1 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(R)-phenyl[[2-(trifluoromethoxy)phenyl]thio]methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



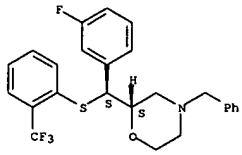
RN 668471-00-9 CAPLUS
CN Benzoic acid, 2-[[(R)-phenyl[(2R)-4-(phenylmethyl)-2-morpholinyl]methyl]thio]-, methyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



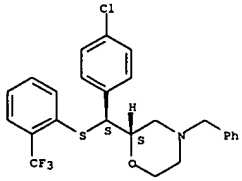
RN 668471-02-1 CAPLUS
CN Morpholine,
2-[(R)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



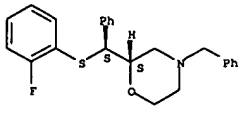
RN 668471-04-3 CAPLUS
CN Morpholine,
2-[(R)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 847687-22-3 CAPLUS
CN Morpholine, 2-[(R)-[(2-fluorophenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

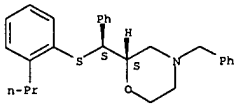
Relative stereochemistry.



RN 847687-24-5 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(R)-phenyl[(2-propylphenyl)thio]methyl]-,

L16 ANSWER 16 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L16 ANSWER 17 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

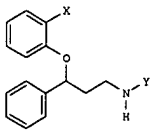
ACCESSION NUMBER: 2005:216659 CAPLUS
DOCUMENT NUMBER: 142:291414
TITLE: Treatment of learning disabilities and motor skills disorder with norepinephrine reuptake inhibitors
INVENTOR(S): Sumner, Calvin Russell
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 304 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005020975	A2	20050310	WO 2004-US25592	20040825
WO 2005020975	A3	20050602		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2530014	A1	20050310	CA 2004-2530014	20040825
EP 1660064	A2	20060531	EP 2004-780430	20040825
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

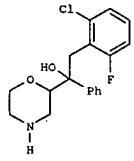
PRIORITY APPLN. INFO.: US 2003-498019P P 20030827
WO 2004-US25592 W 20040825

OTHER SOURCE(S): MARPAT 142:291414
GI

L16 ANSWER 17 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



I



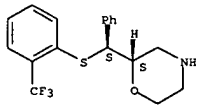
II

AB Provided are methods and medicaments for treating a learning disability or a motor skills disorder, comprising administering to a patient in need of such treatment an effective amount of a selective norepinephrine reuptake inhibitor. The invention discloses the use of atomoxetine, racemic reboxetine, (S,S)-reboxetine, and compds. of formula I [wherein X = alkylthio and Y = alkyl; as described in U.S. patent Number 5,281,624], as well as their pharmaceutically acceptable salts, as the norepinephrine reuptake inhibitors described for treatment purposes. The invention further discloses the preparation of addnl. heterocyclic derivs. (as well as their pharmaceutically acceptable salts) that possess ability to serve as norepinephrine reuptake inhibitors. For instance, morpholine derivative II•HCl was prepared via alkylation of (4-benzyl-morpholin-2-yl)(phenyl)methanone with 2-chloro-6-fluorobenzylmagnesium chloride and subsequent N-debenzylation. The preferred invention compds. exhibited Ki values of less than 500 nM at the norepinephrine transporter (scintillation proximity assay).

IT 668470-56-2P 668470-57-3P 668470-58-4P
668470-59-5P 668470-60-8P 668470-61-9P
668470-62-0P 668470-63-1P 668470-64-2P
668470-65-3P 668470-66-4P 668470-67-5P
668470-68-6P 668470-69-7P 668470-70-0P
668470-71-1P 668470-72-2P 668470-73-3P
668470-74-4P 668470-75-5P 668470-76-6P
668470-77-7P 668470-78-8P 668470-79-9P
847687-23-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic compds. useful as norepinephrine reuptake inhibitors)

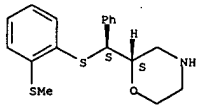
L16 ANSWER 17 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 668470-56-2 CAPLUS
CN Morpholine, 2-[(S)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



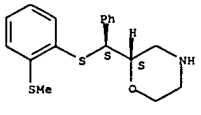
RN 668470-57-3 CAPLUS
CN Morpholine, 2-[(S)-[[2-(methylthio)phenyl]thio]phenylmethyl]-, (2S)-(9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 668470-58-4 CAPLUS
CN Morpholine, 2-[(S)-[[2-(methylthio)phenyl]thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

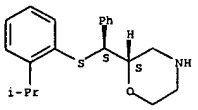
Absolute stereochemistry.



● HCl

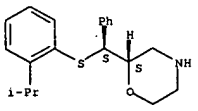
RN 668470-59-5 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethyl)phenyl]thio]phenylmethyl]-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-60-8 CAPLUS
CN Morpholine, 2-[(S)-[(2-(1-methylethyl)phenyl]thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

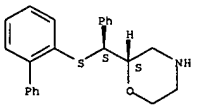
Absolute stereochemistry.



● HCl

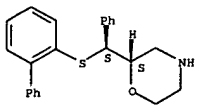
RN 668470-61-9 CAPLUS
CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-62-0 CAPLUS
CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

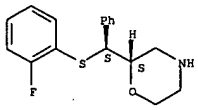
Absolute stereochemistry.



● HCl

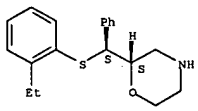
RN 668470-63-1 CAPLUS
CN Morpholine, 2-[(S)-[(2-fluorophenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



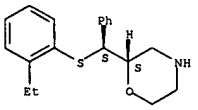
RN 668470-64-2 CAPLUS
CN Morpholine, 2-[(S)-[(2-ethylphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-65-3 CAPLUS
CN Morpholine, 2-[(S)-[(2-ethylphenyl)thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

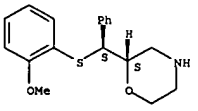
Absolute stereochemistry.



● HCl

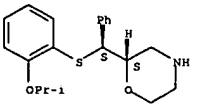
RN 668470-66-4 CAPLUS
CN Morpholine, 2-[(S)-[(2-methoxyphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



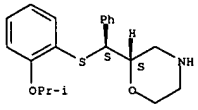
RN 668470-67-5 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-68-6 CAPLUS
CN Morpholine, 2-[(S)-[(2-(1-methylethoxy)phenyl]thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

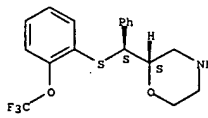
Absolute stereochemistry.



● HCl

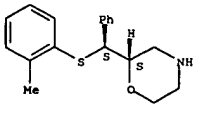
RN 668470-69-7 CAPLUS
CN Morpholine, 2-[(S)-phenyl[[2-(trifluoromethoxy)phenyl]thio]methyl]-, (2S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



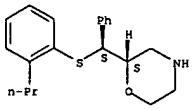
RN 668470-70-0 CAPLUS
CN Morpholine, 2-[(S)-[(2-methylphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



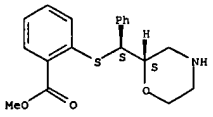
RN 668470-71-1 CAPLUS
CN Morpholine, 2-[(S)-phenyl[(2-propylphenyl)thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



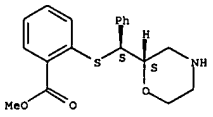
RN 668470-72-2 CAPLUS
CN Benzoic acid, 2-[[(S)-(2S)-2-morpholinylphenylmethyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-73-3 CAPLUS
CN Benzoic acid, 2-[[(S)-(2S)-2-morpholinylphenylmethyl]thio]-, methyl ester,
hydrochloride (9CI) (CA INDEX NAME)

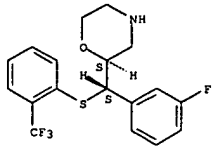
Absolute stereochemistry.



● HCl

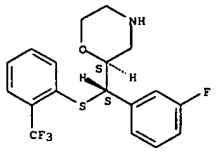
RN 668470-74-4 CAPLUS
CN Morpholine,
2-[(S)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-75-5 CAPLUS
CN Morpholine,
2-[(S)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

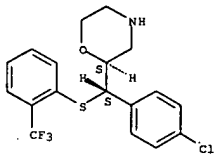
Absolute stereochemistry.



● HCl

RN 668470-76-6 CAPLUS
CN Morpholine,
2-[(S)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

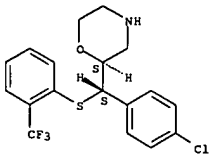
Absolute stereochemistry.



RN 668470-77-7 CAPLUS
CN Morpholine,
2-[(S)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl

]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

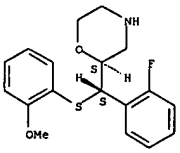
Absolute stereochemistry.



● HCl

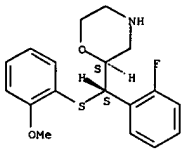
RN 668470-78-8 CAPLUS
CN Morpholine, 2-[(S)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-79-9 CAPLUS
CN Morpholine, 2-[(S)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

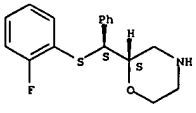
Absolute stereochemistry.



● HCl

RN 847687-23-4 CAPLUS
CN Morpholine, 2-[(S)-[(2-fluorophenyl)thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

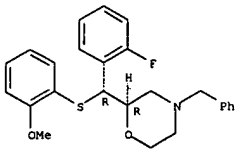


● HCl

IT 667876-61-1P 667876-73-5P 667876-84-8P
667876-86-0P 668470-88-0P 668470-89-1P
668470-90-4P 668470-91-5P 668470-92-6P
668470-95-9P 668470-97-1P 668471-00-9P
668471-02-1P 668471-04-3P 847687-22-3P
847687-24-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclic compds. useful as norepinephrine reuptake inhibitors)

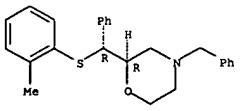
RN 667876-61-1 CAPLUS
CN Morpholine, 2-[(R)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



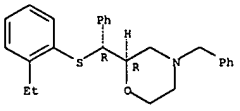
RN 667876-73-5 CAPLUS
CN Morpholine, 2-[(R)-[(2-methylphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



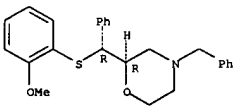
RN 667876-84-8 CAPLUS
CN Morpholine, 2-[(R)-[(2-ethylphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 667876-86-0 CAPLUS
CN Morpholine, 2-[(R)-[(2-methoxyphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

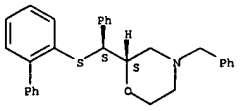
Relative stereochemistry.



RN 668470-88-0 CAPLUS

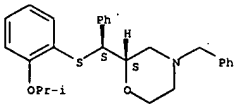
CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



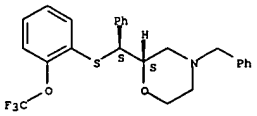
RN 668470-95-9 CAPLUS
CN Morpholine, 2-[(R)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



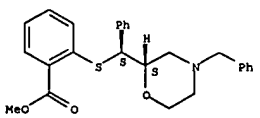
RN 668470-97-1 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(R)-phenyl[[2-(trifluoromethoxy)phenyl]thio]methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



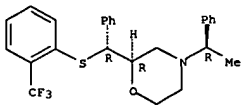
RN 668471-00-9 CAPLUS
CN Benzoic acid, 2-[[(R)-phenyl[(2R)-4-(phenylmethyl)-2-morpholinyl]methyl]thio]-, methyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



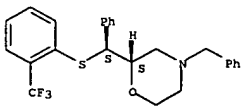
CN Morpholine, 4-[(1R)-1-phenylethyl]-2-[(R)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



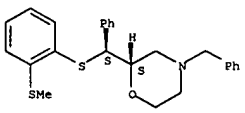
RN 668470-89-1 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(S)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



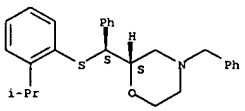
RN 668470-90-4 CAPLUS
CN Morpholine, 2-[(S)-[[2-(methylthio)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-91-5 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethyl)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

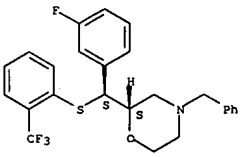
Absolute stereochemistry.



RN 668470-92-6 CAPLUS

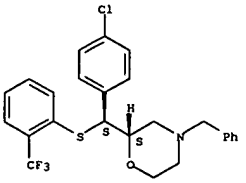
RN 668471-02-1 CAPLUS
CN Morpholine, 2-[(R)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



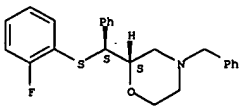
RN 668471-04-3 CAPLUS
CN Morpholine, 2-[(R)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 847687-22-3 CAPLUS
CN Morpholine, 2-[(R)-[(2-fluorophenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

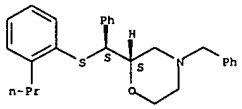
Relative stereochemistry.



RN 847687-24-5 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(R)-phenyl[(2-propylphenyl)thio]methyl]-,

L16 ANSWER 17 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L16 ANSWER 18 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:99358 CAPLUS
DOCUMENT NUMBER: 142:162694
TITLE: Medicinal compositions containing adenosine A2A receptor antagonists and other antidepressants
INVENTOR(S): Kase, Hiroshi; Kobayashi, Minoru; Shiozaki, Shizuo; Mori, Akihisa; Seno, Naoki
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005009444	A1	20050203	WO 2004-JP10758	20040722
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2533117	A1	20050203	CA 2004-2533117	20040722
EP 1655029	A1	20060510	EP 2004-748023	20040722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2006241102	A1	20061026	US 2006-565239	20060119
NO 2006000958	A	20060425	NO 2006-958	20060227

PRIORITY APPLN. INFO.: JP 2003-201549 A 20030725
WO 2004-JP10758 W 20040722

AB It is intended to provide medicinal compns. and the like useful in treating depression which contain a compound having an antagonism to adenosine A2A receptor (for example, (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methyl-3,7-dihydro-1H-purin-2,6-dione) (I) or a pharmacol. acceptable salt thereof together with an antidepressant (for example, a tricyclic antidepressant, a tetracyclic antidepressant, a selective serotonin reuptake inhibitor, a selective noradrenaline reuptake inhibitor, a dopamine reuptake inhibitor, a serotonin/noradrenaline reuptake inhibitor, a monoamine oxidase inhibitor or a serotonin 2 antagonist). The effect of combination of I 0.08 and venlafaxine hydrochloride 5 mg/kg on depression in mice in forced swim test was examined

IT 98769-84-7, Reboxetine mesylate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicinal compns. containing adenosine A2A receptor antagonists and other antidepressants)

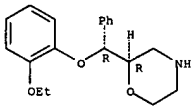
RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

L16 ANSWER 18 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L16 ANSWER 19 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

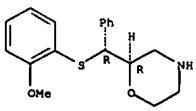
ACCESSION NUMBER: 2005:74686 CAPLUS
DOCUMENT NUMBER: 142:298058
TITLE: Discovery and structure-activity relationships of novel selective norepinephrine and dual serotonin/norepinephrine reuptake inhibitors
AUTHOR(S): Boot, John; Cases, Manuel; Clark, Barry P.; Findlay, Jeremy; Gallagher, Peter T.; Hayhurst, Lorna; Man, Teresa; Montalbetti, Christian; Rathmell, Richard E.; Rudyk, Helene; Walter, Magnus W.; Whatton, Maria; Wood, Virginia
CORPORATE SOURCE: Lilly Research Centre, Eli Lilly & Co. Ltd, Surrey, GU20 6PH, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(3), 699-703
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:298058

AB Novel arylthiomethyl morpholines are potent selective norepinephrine reuptake inhibitors (NERIs) and dual serotonin/norepinephrine reuptake inhibitors (SRI/NERIs). The target compds. were prepared using a stereochem. versatile synthesis featuring an aldol condensation as the key step. One enantiomer of the 2-methoxy-substituted analog was found to be a potent and selective norepinephrine reuptake inhibitor, whereas the opposite enantiomer was a potent dual serotonin/norepinephrine reuptake inhibitor.

IT 667876-44-0P 668470-66-4P
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(stereoselective preparation of (arylthiomethyl)morpholines as selective norepinephrine reuptake inhibitors and dual serotonin/norepinephrine reuptake inhibitors)

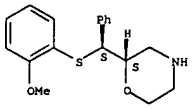
RN 667876-44-0 CAPLUS
CN Morpholine, 2-[(R)-[(2-methoxyphenyl)thio]phenylmethyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



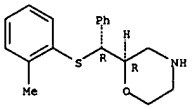
RN 668470-66-4 CAPLUS
CN Morpholine, 2-[(S)-[(2-methoxyphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



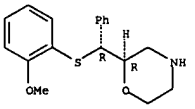
IT 667876-74-6P 667876-87-1P 847740-82-3P
847740-83-4P 847740-84-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(stereoselective preparation of (arylthiomethyl)morpholines as selective
norepinephrine reuptake inhibitors and dual serotonin/norepinephrine reuptake inhibitors)
RN 667876-74-6 CAPLUS
CN Morpholine, 2-[(R)-[(2-methylphenyl)thio]phenylmethyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



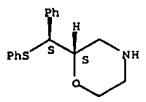
RN 667876-87-1 CAPLUS
CN Morpholine, 2-[(R)-[(2-methoxyphenyl)thio]phenylmethyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



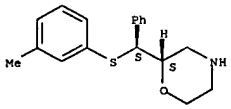
RN 847740-82-3 CAPLUS
CN Morpholine, 2-[(R)-phenyl(phenylthio)methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



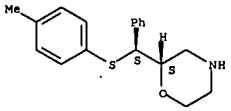
RN 847740-83-4 CAPLUS
CN Morpholine, 2-[(R)-[(3-methylphenyl)thio]phenylmethyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 847740-84-5 CAPLUS
CN Morpholine, 2-[(R)-[(4-methylphenyl)thio]phenylmethyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 20 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1036891 CAPLUS
DOCUMENT NUMBER: 142:16841
TITLE: Treatment of emotional dysregulation
INVENTOR(S): Allen, Albert John; Cloutier, Kathleen Ann; Michelson,
David; Reimherr, Frederick William
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

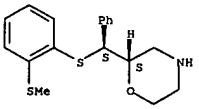
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004103356	A2	20041202	WO 2004-US13005	20040511
WO 2004103356	A3	20050331		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-470752P P 20030515

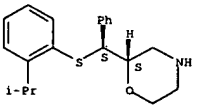
OTHER SOURCE(S): MARPAT 142:16841
AB Provided is a method of treating emotional dysregulation comprising administering to a patient in need of such treatment a selective norepinephrine reuptake inhibitor.
IT 668470-57-3P 668470-59-5P 668470-61-9P
668470-89-1P 668470-93-7P 668470-94-8P
668470-99-3P 800407-96-9P 800407-97-0P
800407-98-1P 800407-99-2P 800408-00-8P
800408-01-9P 800408-02-0P 800408-03-1P
800408-04-2P 800408-05-3P 800408-06-4P
800408-07-5P 800408-08-6P 800408-09-7P
800408-10-0P 800408-11-1P 800408-12-2P
800408-13-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(treatment of emotional dysregulation)
RN 668470-57-3 CAPLUS
CN Morpholine, 2-[(S)-[[2-(methylthio)phenyl]thio]phenylmethyl]-, (2S)-(9CI)
(CA INDEX NAME)

Absolute stereochemistry.



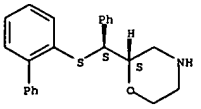
RN 668470-59-5 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethyl)phenyl]thio]phenylmethyl]-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



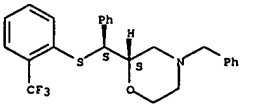
RN 668470-61-9 CAPLUS
CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



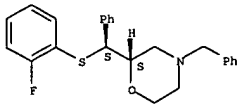
RN 668470-89-1 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(S)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



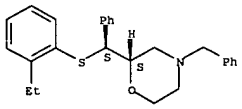
RN 668470-93-7 CAPLUS
CN Morpholine, 2-[(S)-[(2-fluorophenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



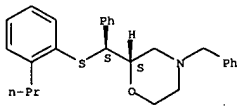
RN 668470-94-8 CAPLUS
CN Morpholine, 2-[(S)-[(2-ethylphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



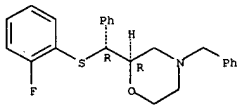
RN 668470-99-3 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(S)-phenyl[(2-propylphenyl)thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 800407-96-9 CAPLUS
CN Morpholine, 2-[(R)-[(2-fluorophenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

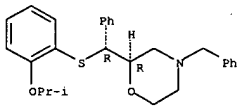
Absolute stereochemistry.



RN 800407-97-0 CAPLUS
CN Morpholine, 2-[(R)-[(2-ethylphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

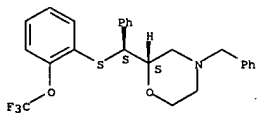
Absolute stereochemistry.

Absolute stereochemistry.



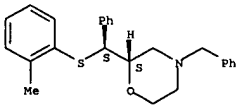
RN 800408-02-0 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(S)-phenyl[(2-(trifluoromethoxy)phenyl]thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



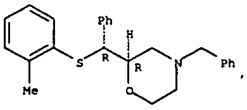
RN 800408-03-1 CAPLUS
CN Morpholine, 2-[(S)-[(2-methylphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

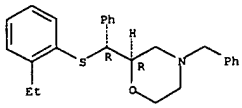


RN 800408-04-2 CAPLUS
CN Morpholine, 2-[(R)-[(2-methylphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

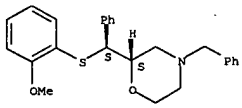


RN 800408-05-3 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(R)-phenyl[(2-propylphenyl)thio]methyl]-,



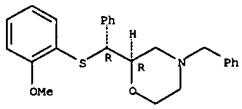
RN 800407-98-1 CAPLUS
CN Morpholine, 2-[(S)-[(2-methoxyphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



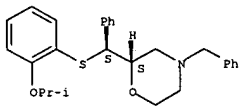
RN 800407-99-2 CAPLUS
CN Morpholine, 2-[(R)-[(2-methoxyphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 800408-00-8 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

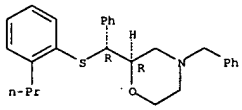
Absolute stereochemistry.



RN 800408-01-9 CAPLUS
CN Morpholine, 2-[(R)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

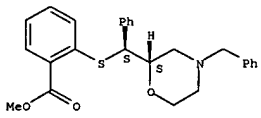
(2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



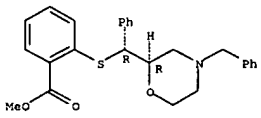
RN 800408-06-4 CAPLUS
CN Benzoic acid, 2-[[(S)-phenyl[(2S)-4-(phenylmethyl)-2-morpholinyl]methyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



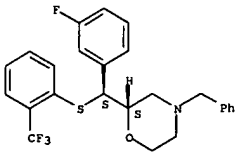
RN 800408-07-5 CAPLUS
CN Benzoic acid, 2-[[(R)-phenyl[(2R)-4-(phenylmethyl)-2-morpholinyl]methyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



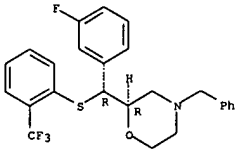
RN 800408-08-6 CAPLUS
CN Morpholine, 2-[(S)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



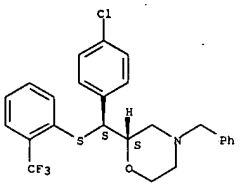
RN 800408-09-7 CAPLUS
CN Morpholine,
2-[(R)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl
]-4-(phenylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 800408-10-0 CAPLUS
CN Morpholine,
2-[(S)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl
]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

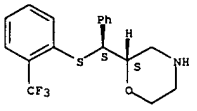
Absolute stereochemistry.



RN 800408-11-1 CAPLUS
CN Morpholine,
2-[(R)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl
]-4-(phenylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

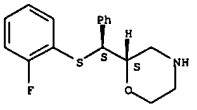
RN 668470-56-2 CAPLUS
CN Morpholine, 2-[(S)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



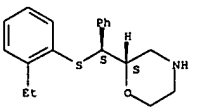
RN 668470-63-1 CAPLUS
CN Morpholine, 2-[(S)-[(2-fluorophenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



RN 668470-64-2 CAPLUS
CN Morpholine, 2-[(S)-[(2-ethylphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA
INDEX NAME)

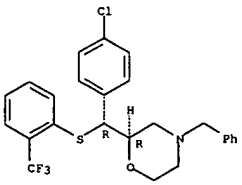
Absolute stereochemistry.



RN 668470-66-4 CAPLUS
CN Morpholine, 2-[(S)-[(2-methoxyphenyl)thio]phenylmethyl]-, (2S)- (9CI)
(CA
INDEX NAME)

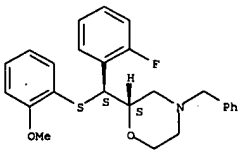
Absolute stereochemistry.

Absolute stereochemistry.



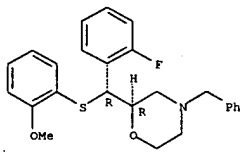
RN 800408-12-2 CAPLUS
CN Morpholine, 2-[(S)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-4-
(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

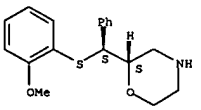


RN 800408-13-3 CAPLUS
CN Morpholine, 2-[(R)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-4-
(phenylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

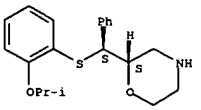


IT 668470-56-2P 668470-63-1P 668470-64-2P
668470-66-4P 668470-67-5P 668470-69-7P
668470-70-0P 668470-71-1P 668470-72-2P
668470-74-4P 668470-76-6P 668470-78-8P
668470-88-0P
RL: SPN (Synthetic preparation); PREP (Preparation)



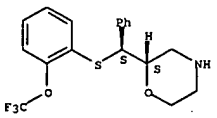
RN 668470-67-5 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-, (2S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



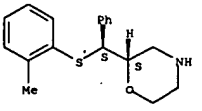
RN 668470-69-7 CAPLUS
CN Morpholine, 2-[(S)-phenyl[[2-(trifluoromethoxy)phenyl]thio]methyl]-,
(2S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



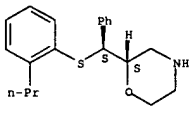
RN 668470-70-0 CAPLUS
CN Morpholine, 2-[(S)-[(2-methylphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



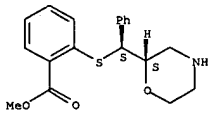
RN 668470-71-1 CAPLUS
CN Morpholine, 2-[(S)-phenyl[(2-propylphenyl)thio]methyl]-, (2S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



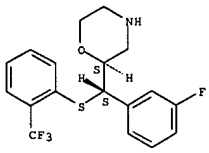
RN 668470-72-2 CAPLUS
CN Benzoic acid, 2-[[(S)-(2S)-2-morpholinylphenylmethyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



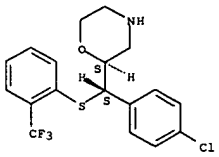
RN 668470-74-4 CAPLUS
CN Morpholine, 2-[(S)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



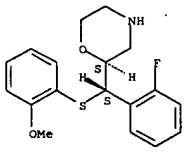
RN 668470-76-6 CAPLUS
CN Morpholine, 2-[(S)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



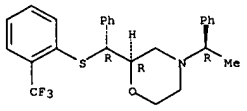
RN 668470-78-8 CAPLUS
CN Morpholine, 2-[(S)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-88-0 CAPLUS
CN Morpholine, 4-[(1R)-1-phenylethyl]-2-[(R)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 21 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:703453 CAPLUS
DOCUMENT NUMBER: 141:388520
TITLE: Studies on the analgesic effects of antidepressants
AUTHOR(S): Suciu, R.; Monea, Marioara
CORPORATE SOURCE: Spitalul Clinic Judetean Targu-Mures, Tirgu-Mures, Rom.
SOURCE: Revista de Medicina si Farmacie (2003), 49(2), 118-124
CODEN: RMFED7; ISSN: 1221-2229
PUBLISHER: Universitatea de Medicina si Farmacie din Targu-Mures
DOCUMENT TYPE: Journal
LANGUAGE: Romanian

AB The effect of noradrenaline and serotonin on pain perception using anti-depressants like sertraline (selective serotonin reuptake inhibitor), tianeptine (selective serotonin reuptake accelerator) and reboxetine (selective noradrenaline reuptake inhibitor) is determined The experiment was carried out on 5 groups of 8 rats each: group 1: placebo, group 2: reboxetine, group 3: reboxetine combined with naloxone, group 4 : tianeptine, group 5: sertraline. To test the analgesic effect of these drugs it was used the hot plate test and tail-flick test. The analgesic effect of reboxetine, tianeptine and sertraline became evident in 20 min after being administrated ($p<0.05$) in both hot plate and tail flick tests. The analgesic effect of reboxetine was antagonized by naloxone ($p<0.05$). This means that the endogenous opioid system might play a role in the analgesic effect of these drugs. The fact that both tianeptine and sertraline have an analgesic effect, although they have opposite mechanism of action might rise some questions about how serotonin really modulates pain but also the role of serotonin in depression.

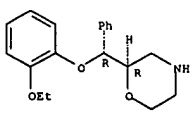
IT 98769-84-7, Edronax
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analgesic effects of antidepressants)

RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.



CM 2

CRN 75-75-2

CMF C H4 O3 S

L16 ANSWER 22 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:634561 CAPLUS
DOCUMENT NUMBER: 141:288417
TITLE: Pharmacokinetics, interaction potential, and therapeutic drug monitoring of modern antidepressants
AUTHOR(S): Haertter, Sebastian
CORPORATE SOURCE: Psychiatrische Klinik und Poliklinik, Klinikum der Johannes Gutenberg-Universitaet Mainz, Mainz, D-55131, Germany
SOURCE: Pharmazie in Unserer Zeit (2004), 33(4), 296-303
CODEN: PHUZBI; ISSN: 0048-3664
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal; General Review
LANGUAGE: German

AB A review is given on some pharmacokinetic characteristics of modern antidepressants. Pharmacokinetics, metabolism, and interaction with other drugs are discussed. Sense and advantages of the therapeutic drug monitoring were evaluated. Citalopram, mirtazapine, reboxetine, sertraline, and venlafaxine are considered.

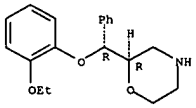
IT 98769-84-7, Edronax
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetics, interaction potential, and therapeutic drug monitoring of modern antidepressants)

RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS

L16 ANSWER 22 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 23 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:182854 CAPLUS
DOCUMENT NUMBER: 140:235726
TITLE: Preparation of benzyl morpholine derivatives capable of inhibiting serotonin and norepinephrin reuptake
INVENTOR(S): Clark, Barry Peter; Gallagher, Peter Thaddeus; Haughton, Helen Louise
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
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CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
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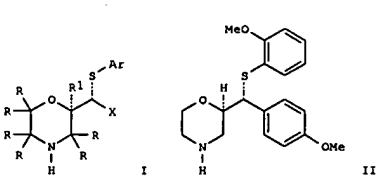
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018440	A1	20040304	WO 2003-US23268	20030818
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003261245	A1	20040311	AU 2003-261245	20030818
EP 1546123	A1	20050629	EP 2003-792992	20030818
EP 1546123	B1	20060531		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 327982	T	20060615	AT 2003-792992	20030818
US 2006052377	A1	20060309	US 2005-524798	20050217

PRIORITY APPLN. INFO.: GB 2002-19685 A 20020823
US 2002-415327P P 20021001
WO 2003-US23268 W 20030818

OTHER SOURCE(S): CASREACT 140:235726; MARPAT 140:235726
GI



I II

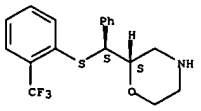
L16 ANSWER 23 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

AB Title compds. I [Ar = (un)substituted Ph optionally substituted with 1-5 substituents selected from alkyl, alkoxy, alkylthio, halo, or (un)substituted phenyl; X = (un)substituted Ph optionally substituted with 1-5 substituents selected from alkyl, alkoxy, or halo ; R1 = H or alkyl; R = independently H or alkyl; each mentioned alkyl may be optionally substituted with one or more halo atoms] and pharmaceutically acceptable salts thereof are prepared and disclosed as inhibitors of serotonin and norepinephrine reuptake. Thus, e.g., II was prepared by condensation of 4-benzyl-2-cyanomorpholine with 4-bromoanisole to provide intermediate [4-methoxyphenyl][4-benzylmorpholin-2-yl]methanone which underwent subsequent reduction, substitution with 2,2'-dimethoxydiphenyldisulfide, debenzylation and resolution via chiral chromataog. to provide II which was converted to its hydrochloride salt. I have been found to exhibit a Ki value less than 100nM at the serotonin transporter and a Ki value less than 100nM at the norepinephrine transporter as determined by scintillation proximity assays.

IT 667876-41-7P
RL: PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(crystal structure; preparation of benzyl morpholine derivs. as selective inhibitors of serotonin and norepinephrine reuptake)

RN 667876-41-7 CAPLUS
CN Morpholine, 2-[(S)-phenyl[(2-(trifluoromethyl)phenyl]thio]methyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

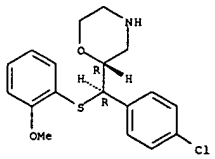


● HCl

IT 667876-96-2P
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
PROC (Process); RACT (Reactant or reagent)
(intermediate; preparation of benzyl morpholine derivs. as selective inhibitors of serotonin and norepinephrine reuptake)

RN 667876-96-2 CAPLUS
CN Morpholine, 2-[(R)-(4-chlorophenyl)[(2-methoxyphenyl)thio]methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

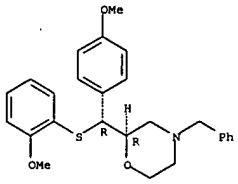
Relative stereochemistry.



IT 667876-57-5P 667876-61-1P 667876-63-3P
667876-64-4P 667876-68-8P 667876-71-3P
667876-73-5P 667876-80-4P 667876-84-8P
667876-86-0P 667876-88-2P 667876-94-0P
667876-95-1P 667877-01-2P 667877-02-3P
667877-06-7P 667877-07-8P 667877-10-3P
667877-15-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of benzyl morpholine derivs. as selective inhibitors of serotonin and norepinephrine reuptake)

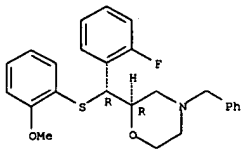
RN 667876-57-5 CAPLUS
CN Morpholine, 2-[(R)-(4-methoxyphenyl)[(2-methoxyphenyl)thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



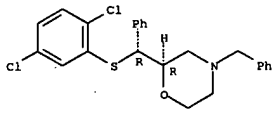
RN 667876-61-1 CAPLUS
CN Morpholine, 2-[(R)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



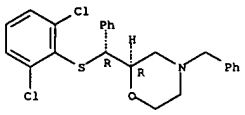
RN 667876-63-3 CAPLUS
CN Morpholine, 2-[(R)-[(2,5-dichlorophenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



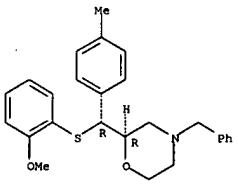
RN 667876-64-4 CAPLUS
CN Morpholine, 2-[(R)-[(2,6-dichlorophenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



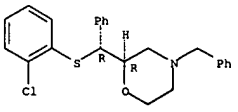
RN 667876-68-8 CAPLUS
CN Morpholine, 2-[(R)-[(2-methoxyphenyl)thio](4-methylphenyl)methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



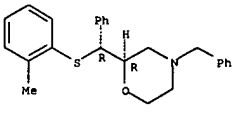
RN 667876-71-3 CAPLUS
CN Morpholine, 2-[(R)-[(2-chlorophenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



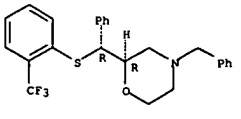
RN 667876-73-5 CAPLUS
CN Morpholine, 2-[(R)-[(2-methylphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



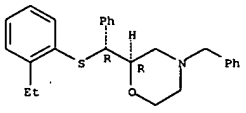
RN 667876-80-4 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(R)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



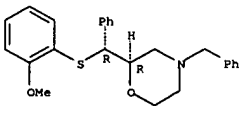
RN 667876-84-8 CAPLUS
CN Morpholine, 2-[(R)-[(2-ethylphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



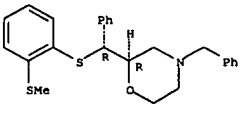
RN 667876-86-0 CAPLUS
CN Morpholine, 2-[(R)-[(2-methoxyphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



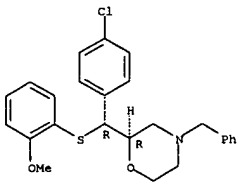
RN 667876-88-2 CAPLUS
CN Morpholine, 2-[(R)-[[2-(methylthio)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



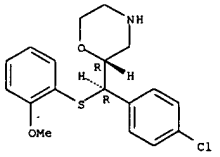
RN 667876-94-0 CAPLUS
CN Morpholine, 2-[(R)-(4-chlorophenyl)[(2-methoxyphenyl)thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 667876-95-1 CAPLUS
CN Morpholine, 2-[(R)-(4-chlorophenyl)[(2-methoxyphenyl)thio]methyl]-, hydrochloride, (2R)-rel- (9CI) (CA INDEX NAME)

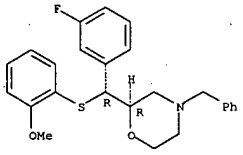
Relative stereochemistry.



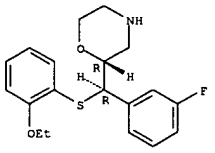
● HCl

RN 667877-01-2 CAPLUS
CN Morpholine, 2-[(R)-(3-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



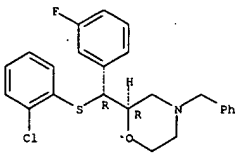
RN 667877-02-3 CAPLUS
CN Morpholine, 2-[(R)-(3-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-,



● HCl

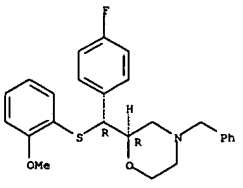
RN 667877-10-3 CAPLUS
CN Morpholine, 2-[(R)-[(2-chlorophenyl)thio](3-fluorophenyl)methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 667877-15-8 CAPLUS
CN Morpholine, 2-[(R)-(4-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

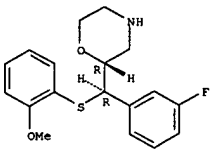
Relative stereochemistry.



IT 667876-62-2P 667876-69-9P 667876-72-4P
667876-74-6P 667876-81-5P 667876-85-9P

hydrochloride, (2R)-rel- (9CI) (CA INDEX NAME)

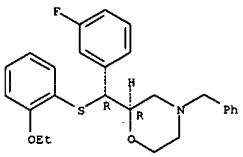
Relative stereochemistry.



● HCl

RN 667877-06-7 CAPLUS
CN Morpholine, 2-[(R)-[(2-ethoxyphenyl)thio](3-fluorophenyl)methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

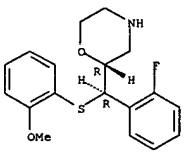


RN 667877-07-8 CAPLUS
CN Morpholine, 2-[(R)-[(2-ethoxyphenyl)thio](3-fluorophenyl)methyl]-, hydrochloride, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

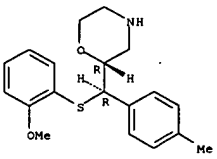
667876-87-1P 667876-89-3P 667877-03-4P
667877-09-0P 667877-11-4P 667877-16-9P
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(prepn. of benzyl morpholine derivs. as selective inhibitors of serotonin and norepinephrine reuptake)
RN 667876-62-2 CAPLUS
CN Morpholine, 2-[(R)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



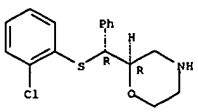
RN 667876-69-9 CAPLUS
CN Morpholine, 2-[(R)-[(2-methoxyphenyl)thio](4-methylphenyl)methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 667876-72-4 CAPLUS
CN Morpholine, 2-[(R)-[(2-chlorophenyl)thio]phenylmethyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

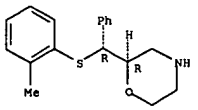
Relative stereochemistry.



RN 667876-74-6 CAPLUS
CN Morpholine, 2-[(R)-[(2-methylphenyl)thio]phenylmethyl]-, (2R)-rel- (9CI)

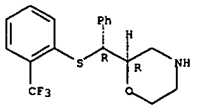
(CA INDEX NAME)

Relative stereochemistry.



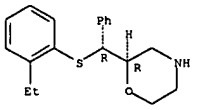
RN 667876-81-5 CAPLUS
CN Morpholine, 2-[(R)-phenyl[(2-(trifluoromethyl)phenyl]thio]methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



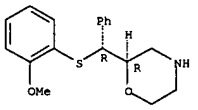
RN 667876-85-9 CAPLUS
CN Morpholine, 2-[(R)-[(2-ethylphenyl)thio]phenylmethyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 667876-87-1 CAPLUS
CN Morpholine, 2-[(R)-[(2-methoxyphenyl)thio]phenylmethyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

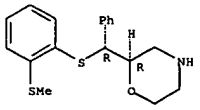
Relative stereochemistry.



RN 667876-89-3 CAPLUS
CN Morpholine, 2-[(R)-[[2-(methylthio)phenyl]thio]phenylmethyl]-, (2R)-rel-

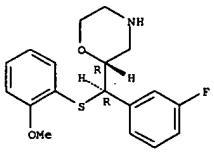
(9CI) (CA INDEX NAME)

Relative stereochemistry.



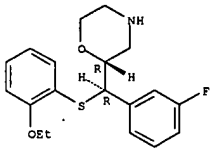
RN 667877-03-4 CAPLUS
CN Morpholine, 2-[(R)-(3-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



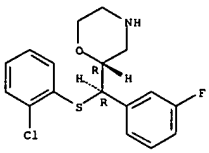
RN 667877-09-0 CAPLUS
CN Morpholine, 2-[(R)-[(2-ethoxyphenyl)thio](3-fluorophenyl)methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



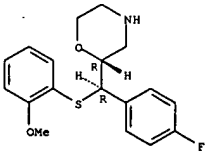
RN 667877-11-4 CAPLUS
CN Morpholine, 2-[(R)-[(2-chlorophenyl)thio](3-fluorophenyl)methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



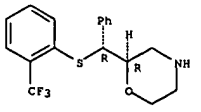
RN 667877-16-9 CAPLUS
CN Morpholine, 2-[(R)-(4-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 667876-40-6P
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of benzyl morpholine derivs. as selective
inhibitors of serotonin and norepinephrine reuptake)
RN 667876-40-6 CAPLUS
CN Morpholine, 2-[(R)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

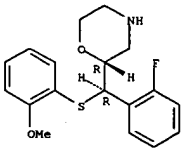


● HCl

IT 667876-27-9P 667876-37-1P 667876-42-8P

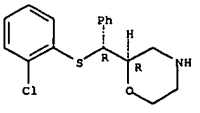
667876-44-0P 667876-50-8P
RL: PAC (Pharmacological activity); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(target compd.; prepn. of benzyl morpholine derivs. as selective inhibitors of serotonin and norepinephrine reuptake)
RN 667876-27-9 CAPLUS
CN Morpholine, 2-[(R)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



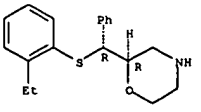
RN 667876-37-1 CAPLUS
CN Morpholine, 2-[(R)-[(2-chlorophenyl)thio]phenylmethyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



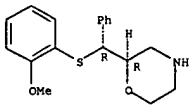
RN 667876-42-8 CAPLUS
CN Morpholine, 2-[(R)-[(2-ethylphenyl)thio]phenylmethyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



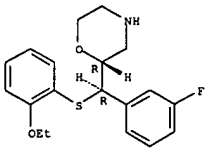
RN 667876-44-0 CAPLUS
CN Morpholine, 2-[(R)-[(2-methoxyphenyl)thio]phenylmethyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



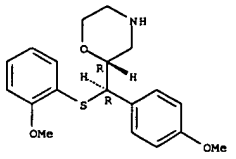
RN 667876-50-8 CAPLUS
CN Morpholine, 2-[(R)-[(2-ethoxyphenyl)thio](3-fluorophenyl)methyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 667876-26-8P 667876-36-0P 667876-39-3P
667876-43-9P 667876-45-1P 667876-46-2P
667876-47-3P 667876-48-4P 667876-49-5P
667876-51-9P 667876-54-2P
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of benzyl morpholine derivs. as selective
inhibitors of serotonin and norepinephrine reuptake)
RN 667876-26-8 CAPLUS
CN Morpholine, 2-[(R)-(4-methoxyphenyl)[(2-methoxyphenyl)thio]methyl]-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

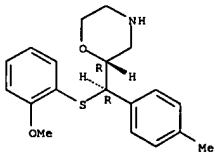
Absolute stereochemistry.



● HCl

RN 667876-36-0 CAPLUS
CN Morpholine, 2-[(R)-[(2-methoxyphenyl)thio](4-methylphenyl)methyl]-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

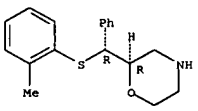
Absolute stereochemistry.



● HCl

RN 667876-39-3 CAPLUS
CN Morpholine, 2-[(R)-[(2-methylphenyl)thio]phenylmethyl]-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

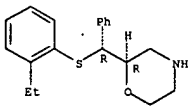
Absolute stereochemistry.



● HCl

RN 667876-43-9 CAPLUS
CN Morpholine, 2-[(R)-[(2-ethylphenyl)thio]phenylmethyl]-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

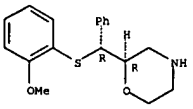
Absolute stereochemistry.



● HCl

RN 667876-45-1 CAPLUS
CN Morpholine, 2-[(R)-[(2-methoxyphenyl)thio]phenylmethyl]-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

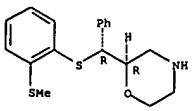
Absolute stereochemistry.



● HCl

RN 667876-46-2 CAPLUS
CN Morpholine, 2-[(R)-[[2-(methylthio)phenyl]thio]phenylmethyl]-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

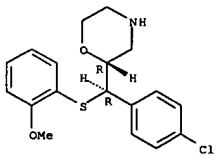
Absolute stereochemistry.



● HCl

RN 667876-47-3 CAPLUS
CN Morpholine, 2-[(R)-(4-chlorophenyl)[(2-methoxyphenyl)thio]methyl]-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

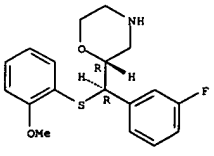
Absolute stereochemistry.



● HCl

RN 667876-48-4 CAPLUS
CN Morpholine, 2-[(R)-(3-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

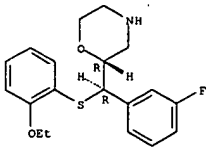
Absolute stereochemistry.



● HCl

RN 667876-49-5 CAPLUS
CN Morpholine, 2-[(R)-[(2-ethoxyphenyl)thio](3-fluorophenyl)methyl]-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

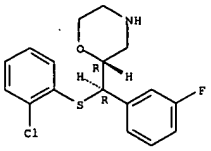
Absolute stereochemistry.



● HCl

RN 667876-51-9 CAPLUS
CN Morpholine, 2-[(R)-[(2-chlorophenyl)thio](3-fluorophenyl)methyl]-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



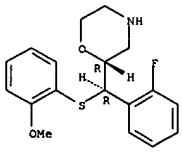
● HCl

RN 667876-54-2 CAPLUS
CN Morpholine, 2-[(R)-(4-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compd.; prepn. of benzyl morpholine derivs. as selective inhibitors of serotonin and norepinephrine reuptake)
RN 667876-28-0 CAPLUS
CN Morpholine, 2-[(R)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

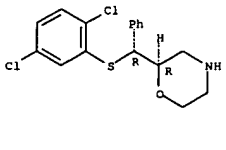
Absolute stereochemistry.



● HCl

RN 667876-30-4 CAPLUS
CN Morpholine, 2-[(R)-[(2,5-dichlorophenyl)thio]phenylmethyl]-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

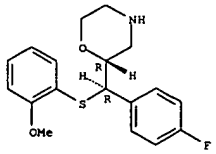
Absolute stereochemistry.



● HCl

RN 667876-34-8 CAPLUS
CN Morpholine, 2-[(R)-[(2,6-dichlorophenyl)thio]phenylmethyl]-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

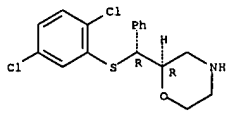
Absolute stereochemistry.



● HCl

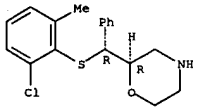
IT 667876-32-6P 667876-52-0P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(target compound; preparation of benzyl morpholine derivs. as selective inhibitors of serotonin and norepinephrine reuptake)
RN 667876-32-6 CAPLUS
CN Morpholine, 2-[(R)-[(2,5-dichlorophenyl)thio]phenylmethyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

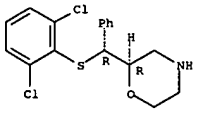


RN 667876-52-0 CAPLUS
CN Morpholine, 2-[(R)-[(2-chloro-6-methylphenyl)thio]phenylmethyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



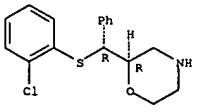
IT 667876-28-0P 667876-30-4P 667876-34-8P
667876-38-2P 667876-53-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU



● HCl

RN 667876-38-2 CAPLUS
CN Morpholine, 2-[(R)-[(2-chlorophenyl)thio]phenylmethyl]-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

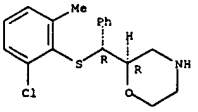
Absolute stereochemistry.



● HCl

RN 667876-53-1 CAPLUS
CN Morpholine, 2-[(R)-[(2-chloro-6-methylphenyl)thio]phenylmethyl]-, hydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



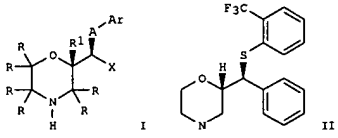
● HCl

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 24 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:182714 CAPLUS
DOCUMENT NUMBER: 140:235724
TITLE: Preparation of benzyl morpholine derivatives capable of selectively inhibiting norepinephrin reuptake
INVENTOR(S): Walter, Magnus Wilhelm; Clark, Barry Peter; Gallagher,
Peter Thaddeus; Haughton, Helen Louise; Rudyk, Helene Catherine Eugenie
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004017977	A2	20040304	WO 2003-US23269	20030818
WO 2004017977	A3	20040401		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003269923	A1	20040311	AU 2003-269923	20030818
EP 1534291	A2	20050601	EP 2003-751812	20030818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006035894	A1	20060216	US 2005-524650	20050217
PRIORITY APPLN. INFO.:			GB 2002-19690 A	20020823
			US 2002-415328P P	20021001
			WO 2003-US23269 W	20030818

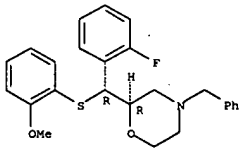
OTHER SOURCE(S): MARPAT 140:235724
GI



AB Title compds. I [A = S or O; Ar = (un)substituted Ph optionally

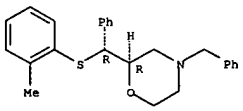
L16 ANSWER 24 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
substituted with 1-5 substituents selected from alkyl, alkoxy, alkylthio, halo, etc.; X = (un)substituted Ph optionally substituted with 1-5 substituents selected from halo, alkyl, alkoxy, cycloalkyl, etc.; R1 = H or alkyl; R = independently H or alkyl; each mentioned alkyl may be optionally substituted with one or more halo atoms; with provisions that when A = O, X = an alkyl group, a cycloalkyl group or cycloalkylmethyl group] and pharmaceutically acceptable salts thereof are prepd. and disclosed as inhibitors of serotonin and norepinephrine reuptake. Thus, e.g., II was prepd. via substitution of
(2S)-2-[(R)-bromo(phenyl)methyl]-4-(phenylmethyl)morpholine (prepn. given) with 2-trifluoromethylthiophenol with subsequent debenzylation. I have been found to exhibit a Ki value less than 500nM at the norepinephrine transporter as detd. by scintillation proximity assays. In addn., I have been found to selectively inhibit norepinephrine transporter relative to the serotonin and dopamine transporters by a factor of at least five.
IT 667876-61-1P 667876-73-5P 667876-86-0P
668470-88-0P 668470-89-1P 668470-90-4P
668470-91-5P 668470-92-6P 668470-93-7P
668470-94-8P 668470-95-9P 668470-97-1P
668470-99-3P 668471-00-9P 668471-02-1P
668471-04-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of benzyl morpholine derivs. as selective inhibitors of norepinephrine reuptake)
RN 667876-61-1 CAPLUS
CN Morpholine, 2-[(R)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 667876-73-5 CAPLUS
CN Morpholine, 2-[(R)-[(2-methylphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

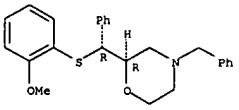
Relative stereochemistry.



RN 667876-86-0 CAPLUS

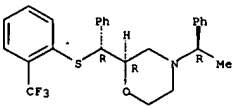
L16 ANSWER 24 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Morpholine, 2-[(R)-[(2-methoxyphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



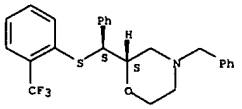
RN 668470-88-0 CAPLUS
CN Morpholine, 4-[(1R)-1-phenylethyl]-2-[(R)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



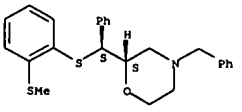
RN 668470-89-1 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(S)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



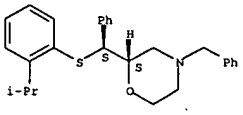
RN 668470-90-4 CAPLUS
CN Morpholine, 2-[(S)-[[2-(methylthio)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



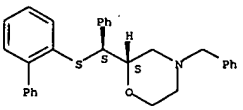
L16 ANSWER 24 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 668470-91-5 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethyl)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



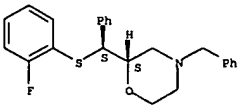
RN 668470-92-6 CAPLUS
CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



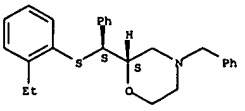
RN 668470-93-7 CAPLUS
CN Morpholine, 2-[(S)-[(2-fluorophenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



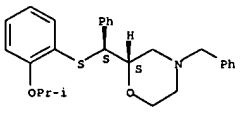
RN 668470-94-8 CAPLUS
CN Morpholine, 2-[(S)-[(2-ethylphenyl)thio]phenylmethyl]-4-(phenylmethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



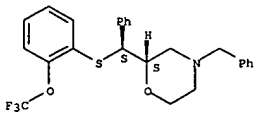
RN 668470-95-9 CAPLUS
CN Morpholine, 2-[(R)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



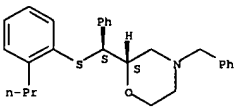
RN 668470-97-1 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(R)-phenyl[[2-(trifluoromethoxy)phenyl]thio]methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



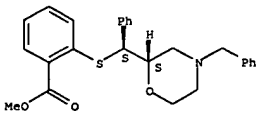
RN 668470-99-3 CAPLUS
CN Morpholine, 4-(phenylmethyl)-2-[(S)-phenyl[(2-propylphenyl)thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



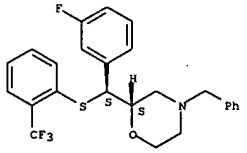
RN 668471-00-9 CAPLUS
CN Benzoic acid, 2-[[(R)-phenyl[(2R)-4-(phenylmethyl)-2-morpholinyl]methyl]thio]-, methyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



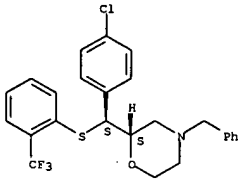
RN 668471-02-1 CAPLUS
CN Morpholine, 2-[(R)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 668471-04-3 CAPLUS
CN Morpholine, 2-[(R)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-4-(phenylmethyl)-, (2R)-rel- (9CI) (CA INDEX NAME)

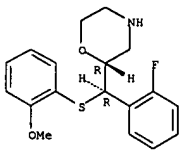
Relative stereochemistry.



IT 667876-62-2P 667876-74-6P 667876-85-9P
667876-87-1P 668470-96-0P 668470-98-2P
668471-01-0P 668471-03-2P 668471-05-4P
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(preparation of benzyl morpholine derivs. as selective inhibitors of norepinephrine reuptake)

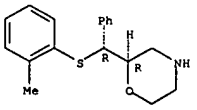
RN 667876-62-2 CAPLUS
CN Morpholine, 2-[(R)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



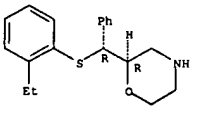
RN 667876-74-6 CAPLUS
CN Morpholine, 2-[(R)-[(2-methylphenyl)thio]phenylmethyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



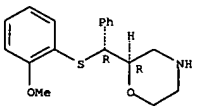
RN 667876-85-9 CAPLUS
CN Morpholine, 2-[(R)-[(2-ethylphenyl)thio]phenylmethyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



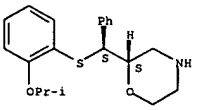
RN 667876-87-1 CAPLUS
CN Morpholine, 2-[(R)-[(2-methoxyphenyl)thio]phenylmethyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



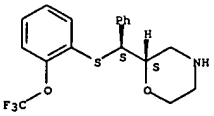
RN 668470-96-0 CAPLUS
CN Morpholine, 2-[(R)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



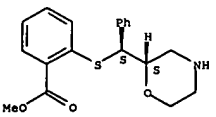
RN 668470-98-2 CAPLUS
CN Morpholine, 2-[(R)-phenyl[[2-(trifluoromethoxy)phenyl]thio]methyl]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 668471-01-0 CAPLUS
CN Benzoic acid, 2-[[(R)-(2R)-2-morpholinylphenylmethyl]thio]-, methyl ester,
rel- (9CI) (CA INDEX NAME)

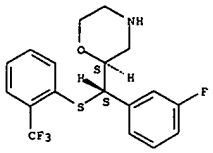
Relative stereochemistry.



RN 668471-03-2 CAPLUS
CN Morpholine, 2-[(R)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl

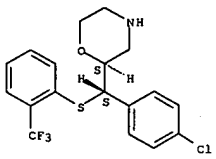
]-, (2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



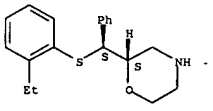
RN 668471-05-4 CAPLUS
CN Morpholine,
2-[(R)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl
]-, (2R)-rel- (9CI) (CA INDEX NAME)

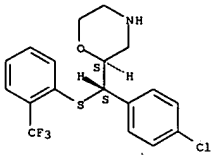
Relative stereochemistry.



IT 668470-64-2P 668470-67-5P 668470-72-2P
668470-74-4P 668470-76-6P 668470-78-8P
RL: PAC (Pharmacological activity); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(target compound; preparation of benzyl morpholine derivs. as selective
inhibitors of norepinephrine reuptake)
RN 668470-64-2 CAPLUS
CN Morpholine, 2-[(S)-[(2-ethylphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

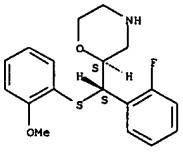
Absolute stereochemistry.





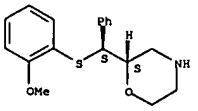
RN 668470-78-8 CAPLUS
CN Morpholine, 2-[(S)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, (2S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 668470-66-4P 668470-69-7P 668470-70-0P
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of benzyl morpholine derivs. as selective
inhibitors of norepinephrine reuptake)
RN 668470-66-4 CAPLUS
CN Morpholine, 2-[(S)-[(2-methoxyphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA
INDEX NAME)

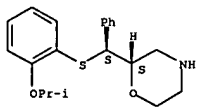
Absolute stereochemistry.



RN 668470-69-7 CAPLUS
CN Morpholine, 2-[(S)-phenyl[[2-(trifluoromethoxy)phenyl]thio]methyl]-, (2S)-
(9CI) (CA INDEX NAME)

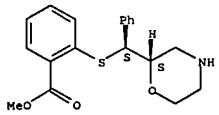
RN 668470-67-5 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-, (2S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



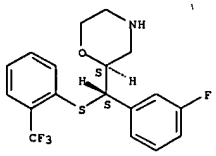
RN 668470-72-2 CAPLUS
CN Benzoic acid, 2-[[(S)-(2S)-2-morpholinylphenylmethyl]thio]-, methyl ester
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-74-4 CAPLUS
CN Morpholine,
2-[(S)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl
]-, (2S)- (9CI) (CA INDEX NAME)

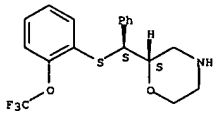
Absolute stereochemistry.



RN 668470-76-6 CAPLUS
CN Morpholine,
2-[(S)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl
]-, (2S)- (9CI) (CA INDEX NAME)

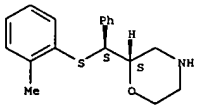
Absolute stereochemistry.

Absolute stereochemistry.



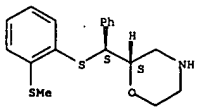
RN 668470-70-0 CAPLUS
CN Morpholine, 2-[(S)-[(2-methylphenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



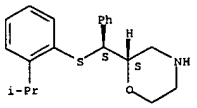
IT 668470-57-3P 668470-59-5P 668470-61-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(target compound; preparation of benzyl morpholine derivs. as selective
inhibitors of norepinephrine reuptake)
RN 668470-57-3 CAPLUS
CN Morpholine, 2-[(S)-[[2-(methylthio)phenyl]thio]phenylmethyl]-, (2S)-
(9CI)
(CA INDEX NAME)

Absolute stereochemistry.



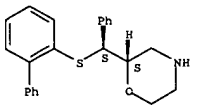
RN 668470-59-5 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethyl)phenyl]thio]phenylmethyl]-, (2S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



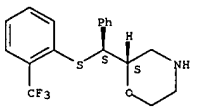
RN 668470-61-9 CAPLUS
CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



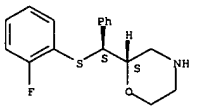
IT 668470-56-2P 668470-58-4P 668470-60-8P
668470-62-0P 668470-63-1P 668470-65-3P
668470-68-6P 668470-71-1P 668470-73-3P
668470-75-5P 668470-77-7P 668470-79-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of benzyl morpholine derivs. as selective
inhibitors of norepinephrine reuptake)
RN 668470-56-2 CAPLUS
CN Morpholine, 2-[(S)-phenyl[[2-(trifluoromethyl)phenyl]thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



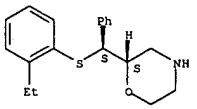
RN 668470-58-4 CAPLUS
CN Morpholine, 2-[(S)-([2-(methylthio)phenyl]thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-65-3 CAPLUS
CN Morpholine, 2-[(S)-[(2-ethylphenyl)thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

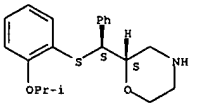
Absolute stereochemistry.



● HCl

RN 668470-68-6 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethoxy)phenyl]thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

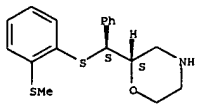
Absolute stereochemistry.



● HCl

RN 668470-71-1 CAPLUS
CN Morpholine, 2-[(S)-phenyl[(2-propylphenyl)thio]methyl]-, (2S)- (9CI) (CA INDEX NAME)

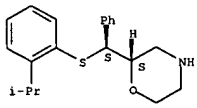
Absolute stereochemistry.



● HCl

RN 668470-60-8 CAPLUS
CN Morpholine, 2-[(S)-[[2-(1-methylethyl)phenyl]thio]phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

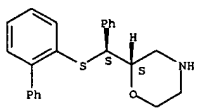
Absolute stereochemistry.



● HCl

RN 668470-62-0 CAPLUS
CN Morpholine, 2-[(S)-([1,1'-biphenyl]-2-ylthio)phenylmethyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

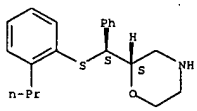
Absolute stereochemistry.



● HCl

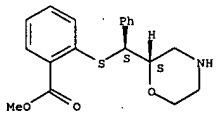
RN 668470-63-1 CAPLUS
CN Morpholine, 2-[(S)-[(2-fluorophenyl)thio]phenylmethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668470-73-3 CAPLUS
CN Benzoic acid, 2-[[(S)-(2S)-2-morpholinylphenylmethyl]thio]-, methyl ester, hydrochloride (9CI) (CA INDEX NAME)

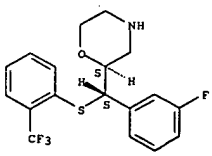
Absolute stereochemistry.



● HCl

RN 668470-75-5 CAPLUS
CN Morpholine, 2-[(S)-(3-fluorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

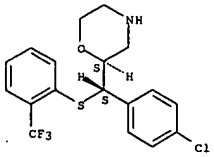
Absolute stereochemistry.



● HCl

RN 668470-77-7 CAPLUS
CN Morpholine, 2-[(S)-(4-chlorophenyl)[[2-(trifluoromethyl)phenyl]thio]methyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

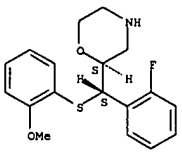
L16 ANSWER 24 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Absolute stereochemistry.



● HCl

RN 668470-79-9 CAPLUS
CN Morpholine, 2-[(S)-(2-fluorophenyl)[(2-methoxyphenyl)thio]methyl]-, hydrochloride, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L16 ANSWER 25 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
mass parts Verapamil HCl and 50 mass parts Eudragit L 100-55, then 160 g of the ground hot melt compd. was mixed with 230 g lactose, 180 g Avicel PH 102, 30 g Explotab and 3 g magnesium stearate and pressed to tablets.

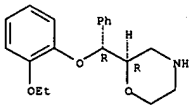
IT 98769-84-7, Reboxetine mesylate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(melt extrusion consisting of salts of active ingredients and (meth)acrylate copolymer)

RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

L16 ANSWER 25 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:696718 CAPLUS
DOCUMENT NUMBER: 139:219346
TITLE: Melt extrusion consisting of salts of active ingredients and (meth)acrylate copolymer
INVENTOR(S): Petereit, Hans-Ulrich; Meier, Christian; Gryczke, Andreas
PATENT ASSIGNEE(S): Roehm G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072083	A2	20030904	WO 2003-EP935	20030130
WO 2003072083	A3	20040408		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10208344	A1	20030904	DE 2002-10208344	20020227
CA 2474691	A1	20030904	CA 2003-2474691	20030130
AU 2003210196	A1	20030909	AU 2003-210196	20030130
EP 1478344	A2	20041124	EP 2003-742925	20030130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007995	A	20041207	BR 2003-7995	20030130
JP 2005526731	T	20050908	JP 2003-570829	20030130
US 2004253314	A1	20041216	US 2004-498829	20040624

PRIORITY APPLN. INFO.:

DE 2002-10208344	A	20020227
WO 2003-EP935	W	20030130

AB The invention relates to a method for producing active ingredient-containing granules or powders involving the following steps: (a) melting a mixture consisting of a pharmaceutically active ingredient and of a (meth)acrylate copolymer, which is comprised of 40-75 weight% of radically polymerized C1-4 alkyl esters of acrylic acid or of methacrylic acid and can be comprised of 25-60 weight% (meth)acrylate monomers having an anionic group in the alkyl radial; (b) extruding the mixture, and; (c) comminuting the extrudate to form a granule or powder. The inventive method is characterized in that the active ingredient is the salt of an alkaline substance, and in that the pH value, which can be measured on the obtained powder or granule, is equal to or less than pH 7.0. The invention also relates to pharmaceutical dosage forms or precursors thereof, which can be produced using the inventive method. Thus a hot melt compound was prepared by coextruding 50

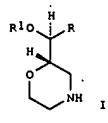
L16 ANSWER 26 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:356092 CAPLUS
DOCUMENT NUMBER: 138:353997
TITLE: Method for the preparation of aryl ethers
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1308443	A2	20030507	EP 2003-2146	19991223
EP 1308443	A3	20031001		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
EP 1140788	A1	20011010	EP 1999-967557	19991223
EP 1140788	B1	20040225		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
IN 2005MN00168	A	20050923	IN 2005-MN168	20050304

PRIORITY APPLN. INFO.:

US 1998-114092P	P	19981229
EP 1999-967557	A3	19991223
WO 1999-US30748	W	19991223
IN 2001-MN483	A3	20010427

OTHER SOURCE(S): CASREACT 138:353997; MARPAT 138:353997
GI



I

AB Aryl ethers I [R, R1 = (un)substituted Ph] are prepared by epoxidn. of an alkenol RCH:CHCH2OH, epoxide cleavage with R1OH, amination N-chloroacetylation, cyclization, and reduction of the resulting morpholinone with a reducing agent, such as BH3, DIBAL, (Me2CH)2AlH, or Na(MeOCH2CH2O)2AlH. Thus, reboxetine was prepared from trans-cinnamyl alc. and 2-EtOC6H4OH in 6 steps.

IT 98769-84-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of aryl ethers from alkenes via epoxides)

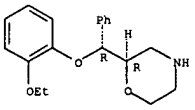
RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

L16 ANSWER 26 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CRN 71620-89-8
CMF C19 H23 N O3

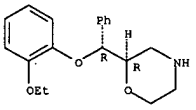
Relative stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

L16 ANSWER 27 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L16 ANSWER 27 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:353282 CAPLUS
DOCUMENT NUMBER: 136:350586
TITLE: The use of selective noradrenaline reuptake inhibitors
for the treatment of tension-type headache
INVENTOR(S): Olesen, Jes; Jensen, Rigmor; Bendtsen, Lars
PATENT ASSIGNEE(S): Head Explorer A.P.S., Den.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002036125	A1	20020510	WO 2001-DK717	20011029
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002013830	A5	20020515	AU 2002-13830	20011029
EP 1333835	A1	20030813	EP 2001-982184	20011029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004048860	A1	20040311	US 2003-415588	20030806

PRIORITY APPLN. INFO.: DK 2000-1638 A 20001031
US 2000-246736P P 20001109
WO 2001-DK717 W 20011029

OTHER SOURCE(S): MARPAT 136:350586

AB This invention relates to the use of selective noradrenaline reuptake inhibitors, in particular reboxetine, for the treatment of tension-type headache. Patients with chronic tension-type headache were treated with reboxetine as the methanesulfonate salt.

IT 98769-84-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of selective noradrenaline reuptake inhibitors for treatment of tension-type headache)

RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.

L16 ANSWER 28 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:771959 CAPLUS
DOCUMENT NUMBER: 136:236927
TITLE: Analysis of reboxetine, a novel antidepressant drug, in pharmaceutical tablets by capillary electrophoresis
and derivative spectrophotometry
AUTHOR(S): Raggi, M. A.; Bugamelli, F.; Sabbioni, C.; Ferranti, A.; Fanali, S.; Volterra, V.
CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Bologna, Bologna, 40126, Italy
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (2002), 27(1-2), 209-215
CODEN: JPBADA; ISSN: 0731-7085
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The recent antidepressant drug reboxetine was quantified in pharmaceutical tablets by derivative spectrophotometry and capillary zone electrophoresis. The feasible sample pretreatment consists of a single extraction with a pH 2.5 phosphate buffer, centrifugation and dilution. For the spectrophotometric assay, the 4th derivative of the absorbance was used which gave satisfactory results in terms of accuracy (mean recovery 99.7%) and precision (mean relative standard deviation 3.4%). The electrophoretic expts. were carried out using the shortest effective length of the capillary (8.5 cm) to obtain a very rapid separation of reboxetine and dibenzepine used as the internal standard. Using a pH 2.5, 50 mM phosphate buffer as the background electrolyte, each anal. lasted <2.5 min. Accuracy (101.3%) and precision (1.5%) were very good.

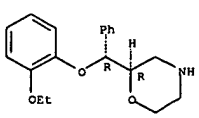
IT 98769-84-7, Davedax
RL: AMX (Analytical matrix); ANST (Analytical study)
(anal. of reboxetine, a novel antidepressant drug, in pharmaceutical tablets by capillary electrophoresis and derivative spectrophotometry)

RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.



CM 2

L16 ANSWER 28 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CRN 75-75-2
CMF C H4 O3 S

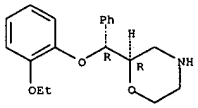
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L16 ANSWER 29 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:565626 CAPLUS
DOCUMENT NUMBER: 135:335263
TITLE: Direct separation of the enantiomers of reboxetine by liquid chromatography on different cellulose- and amylose-based chiral stationary phases
AUTHOR(S): Ficarra, R.; Calabro, M. L.; Tommasini, S.; Melardi, S.; Cutroneo, P.; Ficarra, P.
CORPORATE SOURCE: Department of Pharmaco-Biological Sciences, University
of Catanzaro "Magna Graecia", Complesso ,,Nini Barbieri", Catanzaro, 88021, Italy
SOURCE: Chromatographia (2001), 53(5/6), 261-265
CODEN: CHRGB7; ISSN: 0009-5893
PUBLISHER: Friedrich Vieweg & Sohn Verlagsgesellschaft mbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Racemic reboxetine, (R,S)-2[(R,S)-α-(2-ethoxyphenoxybenzyl)] morpholine methane sulfonate, is a mixture of the (R,R) and (S,S) enantiomers. Separation of the enantiomers of reboxetine by liquid chromatog.
has been investigated on three chiral stationary phases - cellulose tris-(3,5-dimethylphenylcarbamate) (Chiralcel OD); cellulose tris-(phenylcarbamate) (Chiralcel OC), and amylose tris-(3,5-dimethylphenylcarbamate) (Chiralpak AD). On these stationary phases the resolution of the (R,R) and (S,S) enantiomers was highly dependent on mobile
phase composition When Chiralcel OD and OC were used, addition of diethylamine to
the mobile phase greatly improved the separation of the enantiomers. On Chiralpak AD enantiosepn. was achieved without the use of additives. Solute-mobile phase-stationary phase interactions which might participate in the mechanism of enantiorecognition are discussed.
IT 98769-84-7
RL: ANT (Analyte); ANST (Analytical study)
(direct separation of enantiomers of reboxetine by liquid chromatog. on
different cellulose- and amylose-based chiral stationary phases)
RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.



CM 2

L16 ANSWER 29 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L16 ANSWER 30 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:489216 CAPLUS
DOCUMENT NUMBER: 135:81956
TITLE: Transdermal administration of reboxetine
INVENTOR(S): Hoeck, Ulla; Kreilgard, Bo; Kristensen, Helle
PATENT ASSIGNEE(S): Pharmacia AB, Swed.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047503	A1	20010705	WO 2000-SE1972	20001012
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1244431	A1	20021002	EP 2000-971947	20001012
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: SE 1999-4750 A 19991223
WO 2000-SE1972 W 20001012

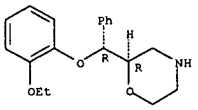
AB A device for transdermal administration of reboxetine, optionally encompassing salts, prodrugs and metabolites thereof, to the use of reboxetine, optionally encompassing salts, prodrugs and metabolites thereof is disclosed. Also disclosed is a method for the manufacturing of a
medicament to be administered transdermally, and methods of treating depression and/or symptoms associated with this condition and/or for treating
addictive disorders and withdrawal syndromes, adjustment disorders, age-associated learning and mental disorders, anorexia nervosa, apathy, attention-deficit disorders due to general medical conditions, attention-deficit hyperactivity disorders, bipolar disorders, bulimia nervosa, chronic fatigue syndrome, conduct disorders, cyclothymic disorders, depression, dysthymic disorders, fibromyalgia and other somatoform disorders, stress incontinence, generalized anxiety disorders, inhalation disorders, an intoxication disorders, obesity, obsessive compulsive disorders and related spectrum disorders, oppositional defiant disorders, and panic disorder. The method also can be applied to treatment of peripheral neuropathy, post-traumatic stress disorder, premenstrual dysphoric disorder, psychotic disorders, seasonal affective disorder, sleep disorder, social phobia, specific developmental disorders and selective serotonin reuptake inhibition (SSRI) "poop out" syndrome and
symptoms associated with these conditions, and/or for obtaining an anti-reserpine and/or noradrenaline reuptake inhibiting effect by transdermal administration of reboxetine, optionally encompassing salts, prodrugs, and metabolites thereof.
IT 98769-84-7
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

L16 ANSWER 30 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(Biological study); PROC (Process)
(transdermal administration of reboxetine for neuropsychiatric therapies)
RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

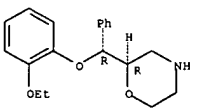
FORMAT

L16 ANSWER 31 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
polyethylene glycol 3350.
IT 98769-84-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reboxetine sustained-release dosage forms)
RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

L16 ANSWER 31 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:208079 CAPLUS
DOCUMENT NUMBER: 134:242664
TITLE: Dosage forms and methods for providing effective reboxetine therapy with once-a-day dosing
INVENTOR(S): Seroff, Sylvia; Yam, Noymi; Ayer, Atul D.; Bhatt, Padmanabh; Desjardin, Michael A.; Lam, Andrew C.; Edgren, David E.; Nixon, Phillip R.
PATENT ASSIGNEE(S): Alza Corporation, USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001019337	A2	20010322	WO 2000-US25333	20000915
WO 2001019337	A3	20010809		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6387403	B1	20020514	US 2000-661976	20000914
CA 2384624	A1	20010322	CA 2000-2384624	20000915
EP 1216031	A2	20020626	EP 2000-963500	20000915
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
TW 233809	B	20050611	TW 2000-89118958	20000915
US 2002146453	A1	20021010	US 2002-87026	20020228
US 6630165	B2	20031007		
PRIORITY APPLN. INFO.:			US 1999-153997P	P 19990915
			US 2000-661976	A1 20000914
			WO 2000-US25333	W 20000915

AB Dosage forms and methods for providing sustained release of reboxetine are provided. The sustained release dosage forms provide therapeutically effective average steady-state plasma reboxetine concns. when administered once per day. This once-a-day dosing regimen results in only one peak plasma reboxetine concentration occurrence in each 24 h period. In addition, the peak plasma reboxetine concentration occurs at a later time following dose administration and exhibits a lesser magnitude than the peak plasma reboxetine concentration that occurs following administration of reboxetine in an immediate-release dosage form. An osmotic dosage forms comprising a bilayer compressed core consisting of a drug layer containing reboxetine methanesulfonate and a push layer in the internal compartment for providing sustained-release of reboxetine were made, and coated with the semipermeable membrane composition containing cellulose acetate (CA 398-10) and

L16 ANSWER 32 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:31317 CAPLUS
DOCUMENT NUMBER: 134:105849
TITLE: Highly selective norepinephrine reuptake inhibitors and methods of using the same
INVENTOR(S): Wong, Erik H. F.; Ahmed, Saeeduddin; Marshall, Robert Clyde; McArthur, Robert; Taylor, Duncan P.; Birgerson, Lars; Cetera, Pasquale
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001001973	A2	20010111	WO 2000-US17256	20000622
WO 2001001973	A3	20020117		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2375908	A1	20010111	CA 2000-2375908	20000622
CA 2375908	C	20060530		
CA 2532330	A1	20010111	CA 2000-2532330	20000622
CA 2543986	A1	20010111	CA 2000-2543986	20000622
AU 200056337	A	20010122	AU 2000-56337	20000622
AU 771258	B2	20040318		
EP 1196172	A2	20020417	EP 2000-941659	20000622
EP 1196172	B1	20060315		
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BR 2000012136	A	20020611	BR 2000-12136	20000622
HU 200201623	A2	20020928	HU 2002-1623	20000622
US 6465458	B1	20021015	US 2000-599213	20000622
JP 2003503450	T	20030128	JP 2001-507467	20000622
NZ 515885	A	20040827	NZ 2000-515885	20000622
EP 1459748	A1	20040922	EP 2004-13379	20000622
EP 1459748	B1	20050413		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
EP 1459749	A1	20040922	EP 2004-13381	20000622
EP 1459749	B1	20051005		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
EP 1459750	A1	20040922	EP 2004-13382	20000622
EP 1459750	B1	20050601		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
EP 1459751	A1	20040922	EP 2004-13383	20000622
EP 1459751	B1	20050914		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

L16 ANSWER 32 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

EP 1493442	A1	20050105	EP 2004-23888		20000622
EP 1493442	B1	20050928			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
EP 1500395	A1	20050126	EP 2004-25513		20000622
EP 1500395	B1	20060308			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
EP 1500396	A1	20050126	EP 2004-25514		20000622
EP 1500396	B1	20050928			
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AT 292971	T	20050415	AT 2004-13379		20000622
AT 296634	T	20050615	AT 2004-13382		20000622
CN 1660108	A	20050831	CN 2004-10104522		20000622
CN 1660109	A	20050831	CN 2004-10104523		20000622
CN 1660110	A	20050831	CN 2004-10104524		20000622
CN 1660111	A	20050831	CN 2004-10104525		20000622
AT 304358	T	20050915	AT 2004-13383		20000622
ES 2239311	T3	20050916	ES 2004-4013379		20000622
AT 305788	T	20051015	AT 2004-13381		20000622
AT 305306	T	20051015	AT 2004-23888		20000622
AT 305307	T	20051015	AT 2004-25514		20000622
ES 2242175	T3	20051101	ES 2004-4013382		20000622
PT 1459751	T	20051130	PT 2004-13383		20000622
NZ 533243	A	20051223	NZ 2000-533243		20000622
ES 2246485	T3	20060216	ES 2004-4013381		20000622
ES 2246487	T3	20060216	ES 2004-4023888		20000622
ES 2246488	T3	20060216	ES 2004-4025514		20000622
EP 1629843	A2	20060301	EP 2005-111705		20000622
EP 1629843	A3	20060315			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
ES 2247572	T3	20060301	ES 2004-4013383		20000622
EP 1632234	A2	20060308	EP 2005-111704		20000622
EP 1632234	A3	20060315			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU					
EP 1632235	A2	20060308	EP 2005-111706		20000622
EP 1632235	A3	20060614			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU					
AT 319453	T	20060315	AT 2004-25513		20000622
AT 320257	T	20060415	AT 2000-941659		20000622
PT 1196172	T	20060531	PT 2000-941659		20000622
ES 2258010	T3	20060816	ES 2000-941659		20000622
ES 2258251	T3	20060816	ES 2004-4025513		20000622
CN 1820754	A	20060823	CN 2005-10136906		20000622
NZ 542816	A	20061222	NZ 2000-542816		20000622
TW 245631	B	20051221	TW 2000-89113086		20000905
US 2002061910	A1	20020523	US 2001-20261		20011214
US 6703389	B2	20040309			
ZA 2001010325	A	20030314	ZA 2001-10325		20011214
NO 2001006406	A	20020219	NO 2001-6406		20011228
US 2002086864	A1	20020704	US 2002-37344		20020104
US 6610690	B2	20030826			
US 2002128173	A1	20020912	US 2002-99334		20020104
US 6642235	B2	20031104			

L16 ANSWER 32 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

US 2003040464	A1	20030227	US 2002-255450		20020926
HK 1049630	A1	20050923	HK 2003-101844		20030314
US 2004058925	A1	20040325	US 2003-669611		20030924
US 2004147614	A1	20040729	US 2004-758864		20040116
AU 2004202096	A1	20040610	AU 2004-202096		20040518
AU 2005220235	A1	20051027	AU 2005-220235		20051007
US 2006128705	A1	20060615	US 2006-349373		20060207
US 2006135520	A1	20060622	US 2006-349022		20060207
US 2006135521	A1	20060622	US 2006-349331		20060207
US 2006142289	A1	20060629	US 2006-348948		20060207
JP 2006143749	A	20060608	JP 2006-45459		20060222
US 2006264436	A1	20061123	US 2006-460775		20060728
JP 2006321815	A	20061130	JP 2006-210418		20060802
PRIORITY APPLN. INFO.:			US 1999-141968P	P	19990701
			US 1999-144131P	P	19990716
			US 1999-158256P	P	19991006
			US 1999-170381P	P	19991213
			US 1999-141986P	P	19990701
			CA 2000-2375908	A3	20000622
			CN 2000-808485	A3	20000622
			CN 2004-10104522	A3	20000622
			EP 2000-941659	A3	20000622
			JP 2001-507467	A3	20000622
			US 2000-599213	A	20000622
			WO 2000-US17256	W	20000622
			US 2002-255450	A3	20020926
			US 2004-758864	A3	20040116
			AU 2004-202096	A3	20040518

AB Methods and compns. for treating humans suffering from, or preventing a human from suffering, a physiol. or psychiatric disease, disorder, or a condition where inhibiting reuptake of norepinephrine is a benefit are disclosed. The compns. comprise a compound having a high pharmacol. selectivity with respect to norepinephrine reuptake sites compared to serotonin reuptake sites. The pharmacol. selectivity of serotonin (Ki)/norepinephrine (Ki) is at least about 5000, preferably about 10,000-12,000. Examples of such compds. include reboxetine in an amount of 6-10 mg/day, and more preferably optically pure (S,S) enantiomer substantially free of (R,R) reboxetine. The methods generally include administration of a therapeutic amount of such compns. Preparation of a medicament from the composition, and uses of the composition in a manufacture of the medicament to treat a human suffering from, or preventing a human from suffering, a physiol. or psychiatric disease, disorder, or condition are also disclosed. For example, (S,S)-reboxetine was about 5-8 fold more

L16 ANSWER 32 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

potent than racemic reboxetine in respect to inhibiting the reuptake of norepinephrine in rats. The selectivity of Ki of serotonin/norepinephrine for (S,S)-reboxetine and racemic reboxetine was 12,770 and 81, resp.

IT 98819-77-3
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(compns. containing highly selective norepinephrine reuptake inhibitors for treatment of psychiatric and other diseases)

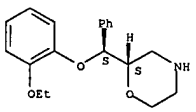
RN 98819-77-3 CAPLUS

CN Morpholine, 2-[(S)-(2-ethoxyphenoxy)phenylmethyl]-, (2S)-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 98819-76-2
CMF C19 H23 N O3

Absolute stereochemistry. Rotation (+).



CM 2

CRN 75-75-2
CMF C H4 O3 S

L16 ANSWER 33 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2000:457014 CAPLUS
DOCUMENT NUMBER:	133:89532
TITLE:	Process for the preparation of aryl ether diastereomers
INVENTOR(S):	Henegar, Kevin E.; Mancini, Sarah Elizabeth; Maisto, Keith Douglas
PATENT ASSIGNEE(S):	Pharmacia & Upjohn Co., USA
SOURCE:	PCT Int. Appl., 53 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000039072	A1	20000706	WO 1999-US30748	19991223
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2349619	A1	20000706	CA 1999-2349619	19991223
EP 1140788	A1	20011010	EP 1999-967557	19991223
EP 1140788	B1	20040225		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9916615	A	20011023	BR 1999-16615	19991223
TR 200101885	T2	20020121	TR 2001-200101885	19991223
US 6376711	B1	20020423	US 1999-469429	19991223
JP 2002533430	T	20021008	JP 2000-590985	19991223
NZ 511452	A	20021126	NZ 1999-511452	19991223
HU 200202144	A2	20021128	HU 2002-2144	19991223
AU 764492	B2	20030821	AU 2000-23819	19991223
AT 260238	T	20040315	AT 1999-967557	19991223
PT 1140788	T	20040730	PT 1999-967557	19991223
ES 2214060	T3	20040901	ES 1999-967557	19991223
CN 1532194	A	20040929	CN 2004-10032369	19991223
CN 1636988	A	20050713	CN 2004-10086926	19991223
IL 144012	A	20051120	IL 1999-144012	19991223
TW 238155	B	20050821	TW 1999-88122940	19991224
IN 2001MN00483	A	20050617	IN 2001-MN483	20010427
ZA 2001003532	A	20020802	ZA 2001-3532	20010502
HK 1066004	A1	20061020	HK 2004-108874	20041110
IN 2005MN00168	A	20050923	IN 2005-MN168	20050304
IN 2005MN00169	A	20051202	IN 2005-MN169	20050304
PRIORITY APPLN. INFO.:			US 1998-114092P	P 19981229
			WO 1999-US30748	W 19991223
			IN 2001-MN483	A3 20010427

OTHER SOURCE(S): CASREACT 133:89532; MARPAT 133:89532

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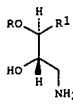
L16 ANSWER 33 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



I

AB Title ethers [I; R,R1 = (un)substituted Ph] were prepared by epoxidn. of R1CH:CHCH2OH and ring opening of the product by ROH followed by O-protection of the primary hydroxyl, sulfonation of the secondary hydroxyl, deprotection of the primary hydroxyl, ring closure displacing the O-sulfonyl group, and amination of the resulting epoxide.

IT 98769-84-7P, Reboxetine mesylate
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for the preparation of aryl ether diastereomers)

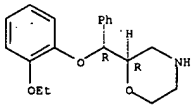
RN 98769-84-7 CAPLUS

CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L16 ANSWER 34 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:514322 CAPLUS
DOCUMENT NUMBER: 131:266516
TITLE: Dose proportionality of reboxetine enantiomers in healthy male volunteers
AUTHOR(S): Rey, E.; Dostert, P.; d'Athis, Ph.; Jannuzzo, M. G.; Poggesi, I.; Olive, G.
CORPORATE SOURCE: Clinical Pharmacology, Hopital Saint-Vincent de Paul, Paris, Fr.
SOURCE: Biopharmaceutics & Drug Disposition (1999), 20(4), 177-181
CODEN: BDDID8; ISSN: 0142-2782
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Reboxetine is a racemic mixture of FCE 22071 and FCE 21684 enantiomers. The pharmacokinetics of the enantiomers of reboxetine were observed to be linear in male healthy subjects (n = 6) after the administration of 1.5, 3, 4.5 mg dose of reboxetine as solns. Kinetic anal. was based on chiral HPLC assay of the enantiomers in plasma collected up to 72 h after each administration. Cmax and AUC were more than double for FCE 22071 (Cmax: 38.3±13.5, 76.6±26.3, 99.8±24.1 ng/mL and AUC∞: 605.8±233.2, 1288.3±796.4, 1780.7±669.3 ng·h/mL for 1.5, 3, 4.5 mg, resp.) than for FCE 21684 (Cmax: 15.2±5.3, 34.6±14.0, 43.1±12.3 ng/mL and AUC∞: 247.0±103.9, 529.1±278.4, 773.0±355.3 ng·h/mL), whatever the administered dose. The half-lives of the enantiomers were similar (FCE 22071: 13.1, 11.0, 12.6 h and FCE 21684: 12.8, 11.2, 12.2 h after 1.5, 3, 4.5 mg, resp.) and not substantially affected by the dose level.

IT 98819-77-3, FCE 21684 105017-39-8, FCE 22071
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(dose proportionality of reboxetine enantiomers in healthy male volunteers)

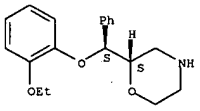
RN 98819-77-3 CAPLUS

CN Morpholine, 2-[(S)-(2-ethoxyphenoxy)phenylmethyl]-, (2S)-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 98819-76-2
CMF C19 H23 N O3

Absolute stereochemistry. Rotation (+).



CM 2

CRN 75-75-2

L16 ANSWER 34 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CMF C H4 O3 S

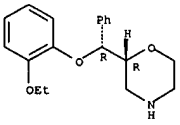
RN 105017-39-8 CAPLUS

CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 105017-38-7
CMF C19 H23 N O3

Absolute stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L16 ANSWER 35 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:359492 CAPLUS
DOCUMENT NUMBER: 127:75474
TITLE: Pharmacokinetics of reboxetine enantiomers in the dog
AUTHOR(S): Frigerio, E.; Benecchi, A.; Brianceschi, G.; Pellizzoni, C.; Poggesi, I.; Strolin Benedetti, M.; Dostert, P.
CORPORATE SOURCE: Pharmacokinetics Metabolism Department, Pharmacia & Upjohn, Milan, Italy
SOURCE: Chirality (1997), 9(3), 303-306
CODEN: CHRLEP; ISSN: 0899-0042
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Reboxetine, (RS)-2-[(RS)-α-(2-ethoxyphenoxy)benzyl]morpholine methanesulfonate, is a racemic compound and consists of a mixture of the (R,R)- and (S,S)-enantiomers. The pharmacokinetics of reboxetine enantiomers were determined in a crossover study in three male beagle dogs. Each animal received the following oral treatments, separated by 1-wk washout period: 10 mg/kg reboxetine, 5 mg/kg (R,R)- and 5 mg/kg (S,S)-. Plasma and urinary levels of the reboxetine enantiomers were monitored ≤48 h post-dosing using an enantiospecific HPLC method with fluorimetric detection (LOQ: 1.1 ng/mL in plasma and 5 ng/mL in urine for each enantiomer). After reboxetine administration, mean tmax was about 1 h for both enantiomers. Cmax and AUC were about 1.5 times higher for the (R,R)- than for the (S,S)-enantiomer, mean values being 704 and 427 ng/mL for Cmax and 2,876,354 and 1,998 ng.h/L for AUC, resp. No differences between the (R,R)- and (S)-enantiomers were observed in t1/2 (3.9 h). Total recovery of the two enantiomers in urine was similar, the Ae (0-48 h) being 1.3 and 1.1% of the enantiomer dose for the (R,R)- and the (S,S)-enantiomers, resp. No marked differences in the main plasma pharmacokinetic parameters were found for either enantiomer on administration of the single enantiomers or reboxetine. No chiral inversion was observed after administration of the sep. enantiomers, as already observed in humans.

IT 98769-84-7, FCE 20124 98819-77-3, FCE 21684 105017-39-8, FCE 22071
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacokinetics of reboxetine enantiomers in dog)

RN 98769-84-7 CAPLUS

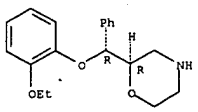
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.

L16 ANSWER 35 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

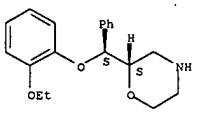
CRN 75-75-2
CMF C H4 O3 S

RN 98819-77-3 CAPLUS
CN Morpholine, 2-[(S)-(2-ethoxyphenoxy)phenylmethyl]-, (2S)-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 98819-76-2
CMF C19 H23 N O3

Absolute stereochemistry. Rotation (+).



CM 2

CRN 75-75-2
CMF C H4 O3 S

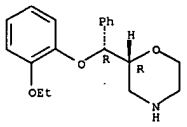
RN 105017-39-8 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-,

L16 ANSWER 35 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 105017-38-7
CMF C19 H23 N O3

Absolute stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

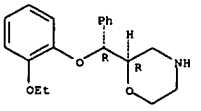
FORMAT

L16 ANSWER 36 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:716659 CAPLUS
DOCUMENT NUMBER: 123:131950
TITLE: Stereoselective and species-dependent kinetics of reboxetine in mouse and rat
AUTHOR(S): Benedetti, Margherita; Frigerio, Enrico; Tocchetti, Paola; Brianceschi, Giannantonio; Castelli, Maria Grazia; Pellizzoni, Cinzia; Dostert, Philippe
CORPORATE SOURCE: Dep. Pharmacokinetics Metabolism, Pharmacia, Milan, Italy
SOURCE: Chirality (1995), 7(4), 285-9
CODEN: CHRLEP; ISSN: 0899-0042
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Reboxetine, (RS)-2-[(RS)-α-(2-ethoxyphenoxy)benzyl]morpholine methanesulfonate, is a racemic compound and consists of a mixture of the (R,R)- and (S,S)-enantiomers. In this study, brain and plasma levels of both enantiomers were determined in mice and rats after oral administration of reboxetine at doses (1.1 mg/kg, mouse; 20 mg/kg, rat) twice the resp. ED50 values in the antireserpine test. Plasma and brain concns. of each enantiomer were measured up to 6 h postdosing using an HPLC method with fluorimetric detection after derivatization with a chiral agent (FLEC). In mice and rats, brain and plasma levels of the (R,R)-enantiomer were always higher than those of the (S,S)-enantiomer. After normalization for dose, the mean AUC0-tz values of both the (R,R)- and (S,S)-enantiomers in mouse brain were bout 23 and 32 times higher than in rat brain, resp. In plasma, the corrected mean AUC0-tz values were about 5 (R,R) and 10 (S,S) times higher in mice than in rats. These results provide evidence for the higher bioavailability and/or lower clearance of both enantiomers in mice than in rats, and for a higher penetration of both enantiomers into mouse brain compared to rat brain.
IT 98769-84-7 98819-77-3 105017-39-8
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(reboxetine stereoselective and species-dependent kinetics in mouse and rat)
RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.



L16 ANSWER 36 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CM 2

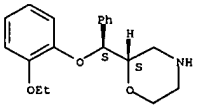
CRN 75-75-2
CMF C H4 O3 S

RN 98819-77-3 CAPLUS
CN Morpholine, 2-[(S)-(2-ethoxyphenoxy)phenylmethyl]-, (2S)-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 98819-76-2
CMF C19 H23 N O3

Absolute stereochemistry. Rotation (+).



CM 2

CRN 75-75-2
CMF C H4 O3 S

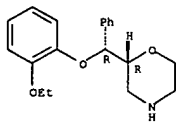
RN 105017-39-8 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 105017-38-7
CMF C19 H23 N O3

Absolute stereochemistry.

L16 ANSWER 36 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 75-75-2
CMF C H4 O3 S

L16 ANSWER 37 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:235242 CAPLUS
DOCUMENT NUMBER: 120:235242
TITLE: Sensitive procedure for the determination of reboxetine enantiomers in human plasma by reversed-phase high-performance liquid chromatography with fluorimetric detection after chiral derivatization with (+)-1-(9-fluorenyl)ethyl chloroformate
AUTHOR(S): Frigerio, E.; Pianezzola, E.; Strolin Benedetti, M.
CORPORATE SOURCE: Research and Development, Pharmacokinetics and Metabolism Department, Farmitalia Carlo Erba, Nerviano, Milan, 20014, Italy
SOURCE: Journal of Chromatography, A (1994), 660(1-2), 351-8
CODEN: JCRAEY; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A sensitive and selective high-performance liquid chromatog. method for the determination of reboxetine enantiomers in human plasma was developed. Although two chiral centers are present in reboxetine, its stereospecific synthesis leads to two rather than four possible enantiomers. After extraction from plasma and reaction with (+)-1-(9-fluorenyl)ethyl chloroformate, reboxetine enantiomers were separated as diastereoisomeric derivs. by reversed-phase high-performance liquid chromatog. (HPLC) and determined by fluorimetric detection. The HPLC anal. time was about 90 min. The linearity, precision, accuracy and limit of quantification of the method were evaluated. No interference from blank plasma sample was observed The suitability of the method for in vivo samples was assessed by the anal. of plasma samples obtained from a healthy male volunteer who had received a single oral dose of 4 mg of reboxetine in tablet form.

IT 98769-84-7, FCE 20124
RL: ANST (Analytical study)
(enantiomeric resolution and determination of, in blood plasma of humans by HPLC with fluorimetric detection after derivatization with fluorenylethyl chloroformate)

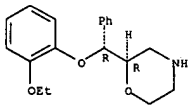
RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.

L16 ANSWER 37 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 75-75-2
CMF C H4 O3 S

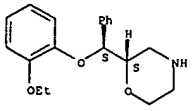
IT 98819-77-3, FCE 21684 105017-39-8, FCE 22071
RL: ANST (Analytical study)
(resolution and determination of, as reboxetine enantiomer in blood plasma of humans, by HPLC with fluorimetric detection after derivatization with fluorenylethyl chloroformate)

RN 98819-77-3 CAPLUS
CN Morpholine, 2-[(S)-(2-ethoxyphenoxy)phenylmethyl]-, (2S)-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 98819-76-2
CMF C19 H23 N O3

Absolute stereochemistry. Rotation (+).



CM 2

CRN 75-75-2
CMF C H4 O3 S

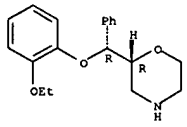
L16 ANSWER 37 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 105017-39-8 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 105017-38-7
CMF C19 H23 N O3

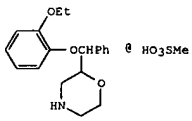
Absolute stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

L16 ANSWER 38 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:187425 CAPLUS
DOCUMENT NUMBER: 116:187425
TITLE: Comparison of the disposition and of the metabolic pattern of Reboxetine, a new antidepressant, in the rat, dog, monkey and man
AUTHOR(S): Cocchiara, G.; Battaglia, R.; Pevarello, P.; Strolin Benedetti, M.
CORPORATE SOURCE: Erbamont Group, Farmitalia Carlo Erba Res. Dev., Milan, I-20159, Italy
SOURCE: European Journal of Drug Metabolism and Pharmacokinetics (1991), 16(3), 231-9
CODEN: EJDPD2; ISSN: 0398-7639
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



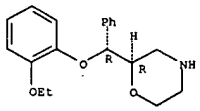
I

AB The purpose of this study was to compare the disposition and the metabolic pattern of Reboxetine (I) in several species, including man. [14C]I was given orally to the rat, the dog, the monkey (5 mg/kg) and man (2 and 4 mg/kg). Radioactivity was eliminated both by the renal and fecal route in the rat and the dog, mainly in urine in the monkey and man. I was extensively metabolized. A number of urinary metabolites were quantified by radio-HPLC and tentatively identified by comparison with the retention times of reference compds. Suggested routes of metabolic transformation are: 2-O-dealkylation; hydroxylation of the ethoxyphenoxy ring; oxidation of the morpholine ring; morphine ring-opening; and combinations of these. Metabolites were partially or completely conjugated with glucuronic acid and/or sulfuric acid.
IT 98769-84-7, Reboxetine mesylate
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(comparative disposition and metabolic pattern of, in laboratory animals and humans)
RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

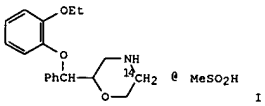
L16 ANSWER 38 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Relative stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

L16 ANSWER 39 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:471507 CAPLUS
DOCUMENT NUMBER: 115:71507
TITLE: Preparation of 2-[α-(2-ethoxyphenoxy)benzyl][5-14C]morpholine methanesulfonate ([14C]reboxetine), a new antidepressant agent
AUTHOR(S): Angiuli, Patrizia; Fontana, Erminia; Vicario, Gian Piero
CORPORATE SOURCE: Metab. Pharmacokinet. Dep., Farmitalia Carlo Erba S.r.l., Milan, 20124, Italy
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1991), 29(5), 607-11
CODEN: JLCRD4; ISSN: 0362-4803
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 115:71507
GI

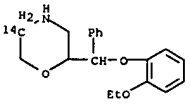


I

AB Title compound I was prepared by cyclization of CH(OH)(CHRR1)CH2NH18COCH2Cl (R = 2-ethoxyphenoxy, R1 = Ph) to give the morpholone which underwent reduction I was 98% radiochem. pure and has a specific radioactivity of 988 MBq/mmol.
IT 135020-16-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 135020-16-5 CAPLUS
CN Morpholine-3-14C, 6-[(2-ethoxyphenoxy)phenylmethyl]-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 135020-15-4
CMF C19 H23 N O3



CM 2

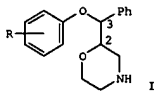
L16 ANSWER 39 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CRN 75-75-2
CMF C H4 O3 S

L16 ANSWER 40 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:591107 CAPLUS
DOCUMENT NUMBER: 105:191107
TITLE: Enantiomers of phenoxy derivatives of benzylmorpholine
and its salts, and pharmaceuticals containing them
INVENTOR(S): Melloni, Piero; Torre, Arturo Della; Carniel, Giovanni; Rossi, Allessandro
PATENT ASSIGNEE(S): Farmitalia Carlo Erba S.p.A., Italy
SOURCE: Ger. Offen., 36 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3540093	A1	19860528	DE 1985-3540093	19851112
GB 2167407	A	19860529	GB 1984-29546	19841122
GB 2167407	B	19880511		
JP 61129174	A	19860617	JP 1985-258816	19851120
JP 06067916	B	19940831		
FR 2573425	A1	19860523	FR 1985-17324	19851122
FR 2573425	B1	19881223		

PRIORITY APPLN. INFO.: GB 1984-29546 A 19841122

OTHER SOURCE(S): CASREACT 105:191107; MARPAT 105:191107
GI


I

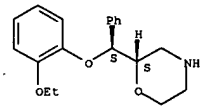
AB 2R,3R- Or 2S,3S-enantiomers of (phenoxybenzyl)morpholines I (R = C1-6 alkoxy, trihalomethyl) and their salts, useful as antidepressants, are prepared Thus, (+)-(2S,3R)-phenylglycidic acid D(+)-α-methylphenethylamine was reduced with NaBH4 to give (+)2R,3R-cinnamic alc.
2,3-epoxide, which was reacted with 2-ethoxyphenol to give (+)2R,3S-3-(2-ethoxyphenoxy)-1,2-dihydroxy-3-phenylpropane. The diol was reacted with 4-nitrobenzoyl chloride, the product was mesylated and then converted to (-)2S,3S-3-(2-ethoxyphenoxy)-3-phenylpropane-1,2-epoxide, which underwent successively ammonolysis, chloroacetylation, cyclization, and reduction to give (+)2S,3S-2-[α-(2-ethoxyphenoxy)benzyl]morpholine-MeSO3H (II). A tablet was formulated containing II 5, lactose 143, starch 45,
talc 5, and Mg stearate 2 mg.
IT 98819-77-3P 105017-39-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antidepressant)
RN 98819-77-3 CAPLUS

L16 ANSWER 40 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Morpholine, 2-[(S)-(2-ethoxyphenoxy)phenylmethyl]-, (2S)-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 98819-76-2
CMF C19 H23 N O3

Absolute stereochemistry. Rotation (+).



CM 2

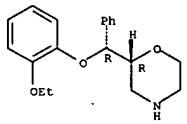
CRN 75-75-2
CMF C H4 O3 S

RN 105017-39-8 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 105017-38-7
CMF C19 H23 N O3

Absolute stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

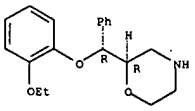
L16 ANSWER 40 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

IT 98769-84-7
RL: PROC (Process)
(resolution of)
RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

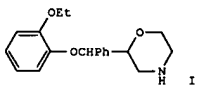
Relative stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S

L16 ANSWER 41 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:578207 CAPLUS
DOCUMENT NUMBER: 103:178207
TITLE: Configurational studies on 2-[α-(2-ethoxyphenoxy)benzyl]morpholine FCE 20124
AUTHOR(S): Melloni, P.; Della Torre, A.; Lazzari, E.; Mazzini, G.; Meroni, M.
CORPORATE SOURCE: Ric. Sviluppo Chim., Farm. Carlo Erba S.p.A., Milan, 20159, Italy
SOURCE: Tetrahedron (1985), 41(7), 1393-9
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 103:178207
GI

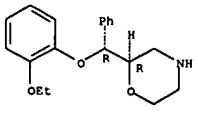

I

AB The relative configuration of the diastereoisomers of (±)-2-[α-(2-ethoxyphenoxy)benzyl]morpholine (I) is determined by a synthesis involving
regio- and stereospecific reactions. (RS,RS)-I was separated into its (+)-
and (-)-enantiomers both by crystallization of the optically active mandelate salt
and by a multi-step synthesis from (+)-(2S,3R)-3-phenylglycidic acid.
IT 98769-84-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and resolution of)
RN 98769-84-7 CAPLUS
CN Morpholine, 2-[(R)-(2-ethoxyphenoxy)phenylmethyl]-, (2R)-rel-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 71620-89-8
CMF C19 H23 N O3

Relative stereochemistry.



CM 2

L16 ANSWER 41 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

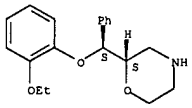
CRN 75-75-2
CMF C H4 O3 S

IT 98819-77-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 98819-77-3 CAPLUS
CN Morpholine, 2-[(S)-(2-ethoxyphenoxy)phenylmethyl]-, (2S)-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 98819-76-2
CMF C19 H23 N O3

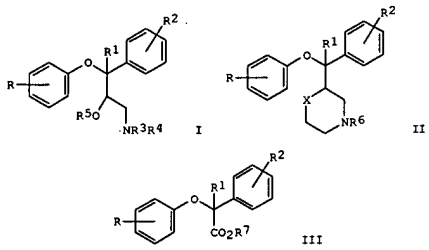
Absolute stereochemistry. Rotation (+).



CM 2

CRN 75-75-2
CMF C H4 O3 S

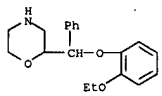
L16 ANSWER 42 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:24560 CAPLUS
DOCUMENT NUMBER: 102:24560
TITLE: Potential antidepressant agents. α-Aryloxybenzyl derivatives of ethanolamine and morpholine
AUTHOR(S): Melloni, Piero; Carniel, Giovanni; Della Torre, Arturo; Bonsignori, Alberto; Buonamici, Matilde; Pozzi, Ottorino; Ricciardi, Sante; Rossi, Alessandro C.
CORPORATE SOURCE: Farmitalia C. Erba S.p.A., Milan, 20159, Italy
SOURCE: European Journal of Medicinal Chemistry (1984), 19(3),
235-42
CODEN: EJMCA5; ISSN: 0223-5234
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 102:24560
GI



AB The title compds. I and II (R = Me, H, Cl, MeO, methylenedioxy; R1 = H, Me, R2 = H, MeO, Cl; R3 = H, Me, Me2CH; R4, R5 = H, Me; R6 = H, Me, Ac, MeNHCO, etc.; X = O, CH2, MeN) were prepared as antidepressants from phenoxyacetates III (R7 = Et). Thus, III (R = 2-MeO, R1 = R2 = R7 = H) was treated with carbonyldiimidazole and nitromethane sodium salt to give the nitro enolate, which was reduced by H2/PtO2 to give 2 diastereoisomers of I (R = 2-MeO, R1-R5 H). II (R = 2-EtO, R1 = R2 = R6 = H; X = O) showed outstanding activity in the antireserpine test when compared with Imipramine, Desipramine and Viloxazine.
IT 93851-87-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antidepressant activity of)
RN 93851-87-7 CAPLUS
CN Morpholine, 2-[(2-ethoxyphenoxy)phenylmethyl]-, methanesulfonate (9CI) (CA INDEX NAME)

L16 ANSWER 42 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CM 1

CRN 93851-86-6
CMF C19 H23 N O3



CM 2

CRN 75-75-2
CMF C H4 O3 S

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	225.10	607.75

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-32.76	-33.54

STN INTERNATIONAL LOGOFF AT 08:28:17 ON 13 MAR 2007